



# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 180159

TO: Shirley Gembah  
Art Unit: 1614  
Location: REM-3A44/3C70  
Serial Number: 10/712423

Monday, March 13, 2006

From: Beverly Shears  
Location: Biotech-Chem Library  
REM 1A54  
Phone: 571-272-2528  
beverly.shears@uspto.gov

### Search Notes

Shirley,

If you have any questions regarding the search strategy, pls. contact me.

Beverly

10/712423

FILE 'REGISTRY' ENTERED AT 12:30:53 ON 03 MAR 2006  
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STRUCTURE FILE UPDATES: 2 MAR 2006 HIGHEST RN 875740-40-2  
DICTIONARY FILE UPDATES: 2 MAR 2006 HIGHEST RN 875740-40-2

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

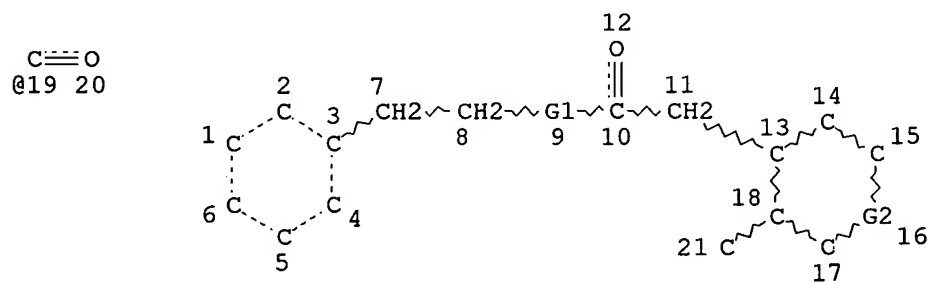
Structure search iteration limits have been increased. See HELP SLIMITS  
for details.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

L1

STR



VAR G1=O/S/CH2/19  
VAR G2=O/S/CH2/19  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 21

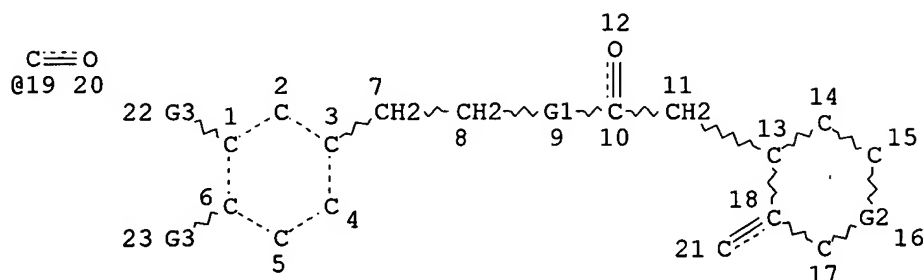
Searcher : Shears 571-272-2528

10/712423

STEREO ATTRIBUTES: NONE

L2 ( 132) SEA FILE=REGISTRY SSS FUL L1

L3 STR



VAR G1=O/S/CH2/19

VAR G2=O/S/CH2/19

VAR G3=OH/N/S

NODE ATTRIBUTES:

CONNECT IS X2 RC AT 15

CONNECT IS M3 RC AT 17

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L4 32 SEA FILE=REGISTRY SUB=L2 SSS FUL L3

100.0% PROCESSED 127 ITERATIONS

32 ANSWERS

SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 12:30:53 ON 03 MAR 2006

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FILE COVERS 1907 - 3 Mar 2006 VOL 144 ISS 11

FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)

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10/712423

L5 540 SEA ABB=ON PLU=ON L4  
L6 30 SEA ABB=ON PLU=ON L5 AND (?CANCER? OR ?CARCIN? OR  
?TUMOUR? OR ?TUMOR? OR ?NEOPLAS?)  
L7 13 SEA ABB=ON PLU=ON L6 NOT (PY=>2002 OR PD=>20021209)

E3 THROUGH E4 ASSIGNED

L7 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:296202 CAPLUS

DOCUMENT NUMBER: 136:293669

TITLE: Oleuropein and related degradation compounds of  
olives with antioxidant activity

AUTHOR(S): Schmandke, Horst

CORPORATE SOURCE: Bergholz-Rehbrucke, 14558, Germany

SOURCE: Ernaehrungs-Umschau (2001), 48(12), 490-492

CODEN: ERUMAT; ISSN: 0014-021X

PUBLISHER: Umschau Zeitschriftenverlag Breidenstein

DOCUMENT TYPE: Journal; General Review

LANGUAGE: German

AB A review. Fresh olives contain the bitter principle oleuropein, its aglycon and the degradation products elenolic acid glucoside, hydroxytyrosol and its glucosides. During the debittering of olives by Spanish-, Californian- or Greek-style processing oleuropein further on is degraded to the earlier mentioned compds. who - together with the residual oleuropein - finally are being removed from the olives into the processing brine by diffusion. Non raffinated olive oils (extra virgin and virgin oils) contain beside small contents of oleuropein first of all his aglycon, the corresponding dialdehydic form (oleuropeindial), small concns. of decarbomethoxyoleuropeindial and hydroxytyrosol. By oil raffination all phenolic compds. are eliminated vastly. Oleuropein is poorly and hydroxytyrosol dose-dependently absorbed. They are excreted urinarilly as glucuronide conjugates of hydroxytyrosol and 4-hydroxy-3-methoxy-phenethanol. In vitro studies demonstrated that oleuropein and hydroxytyrosol have antioxidant activities in cell-free model solns., in LDL, platelets, leukocytes, neutrophils and epithelial intestinal cells. This antioxidant effect inhibits the arachidonic acid metabolism by inhibition of the 5- and 12-lipoxygenase activities and the formation of 5- and 12-hydroxy-5,8,10,14-eicosatetraenoic acid, F2-isoprostane, leukotriene B4 and thromboxane B2. The platelet aggregation is reduced. These facts are confirmed by a dose-dependent decrease of urinary excretion of F2-isoprostane in humans. In vitro oleuropein shows cytostatic activity against McCoy cells, indicating an anti-tumoral capacity. Oleuropein inhibits cytochrome P 450 and can therefore effect the bioavailability of drugs.

IT 32619-42-4, Oleuropein

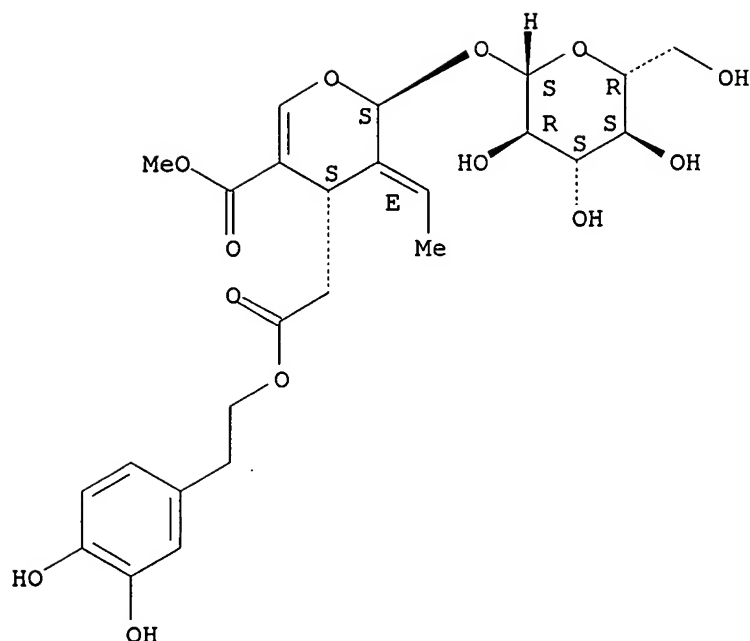
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(oleuropein and related degradation compds. of olives with antioxidant activity)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-  
3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester,  
(2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:818973 CAPLUS

DOCUMENT NUMBER: 137:15715

TITLE: The inhibitory effects of compounds from olive leaf on **tumor** necrosis factor production and on  $\beta$ -hexosaminidase release

AUTHOR(S): Nishibe, Sansei; Han, Yingmei; Noguchi, Yukari; Ueda, Hiroshi; Yamazaki, Masatoshi; Mizutani, Kenji; Kambara, Toshimitsu; Kishida, Naoko

CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido, 061-0293, Japan

SOURCE: Natural Medicines (Tokyo, Japan) (2001), 55(4), 205-208

CODEN: NMEDEO; ISSN: 1340-3443

PUBLISHER: Japanese Society of Pharmacognosy

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The extraction and isolation of olive leaf gave luteolin 7-O-glucoside, luteolin 4'-O-glucoside and oleuropein as the major components. The inhibitory effects of these compds. on **tumor** necrosis factor (TNF- $\alpha$ ) production and on  $\beta$ -hexosaminidase release from rat basophilic leukemia (RBL-2H3) cells, which were both recently found to be linked to allergic reaction, were examined. Oleuropein showed a potent inhibitory effect on TNF- $\alpha$  production. Luteolin 4'-O-glucoside showed a strong inhibitory effect on  $\beta$ -hexosaminidase release (IC<sub>50</sub>:17.1  $\mu$ g/mL).

IT **32619-42-4P**, Oleuropein

RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)

10/712423

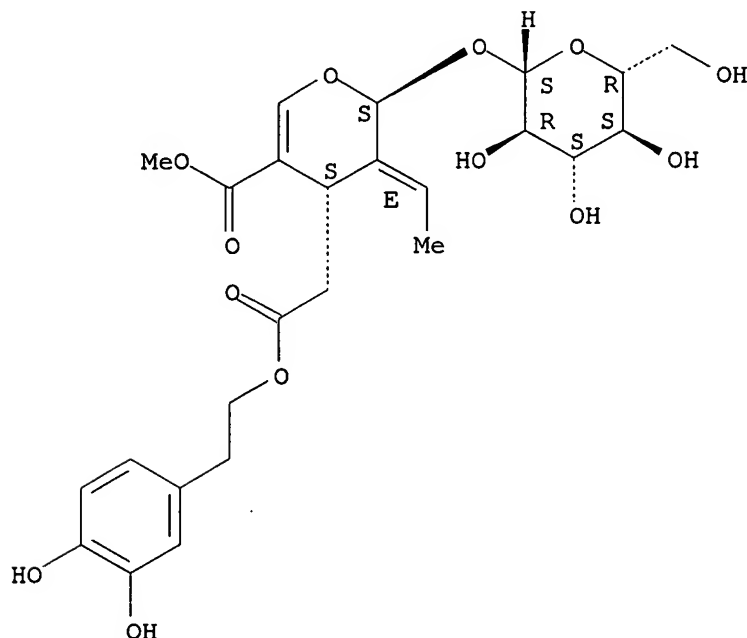
(inhibitory effects of compds. from olive leaf on tumor  
necrosis factor production and on  $\beta$ -hexosaminidase release)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-  
3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester,  
(2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE  
RE FORMAT

L7 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:490007 CAPLUS

DOCUMENT NUMBER: 135:226053

TITLE: Characterization of Phenolic Compounds in Virgin  
Olive Oil and Their Effect on the Formation of  
**Carcinogenic**/Mutagenic Heterocyclic Amines  
in a Model System

AUTHOR(S): Monti, Simona M.; Ritieni, Alberto; Sacchi,  
Raffaele; Skog, Kerstin; Borgen, Eva; Fogliano,  
Vincenzo

CORPORATE SOURCE: Dipartimento di Scienza degli Alimenti, Università  
di Napoli Federico II, Naples, 80055, Italy

SOURCE: Journal of Agricultural and Food Chemistry (2001),  
49(8), 3969-3975

CODEN: JAFCAU; ISSN: 0021-8561

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mutagenic heterocyclic amines (HAs) are formed at low levels during

Searcher : Shears 571-272-2528

cooking of meat and fish, and some of them are considered to be possible human **carcinogens**. The formation of HAs may be affected by the presence of synthetic or naturally occurring antioxidants. In the present study the effect of virgin olive oil (VOO) phenolic compds., identified and quantified by LC-MS, on the formation of HAs in a model system was evaluated. An aqueous solution of creatinine, glucose, and glycine was heated in the presence of 2 samples of VOO differing only in the composition of phenolic compds. The addition of VOO to the model system inhibited the formation of 2-amino-3-methylimidazo[4,5-f]quinoxaline (IQx), 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx), and 2-amino-3,7,8-trimethylimidazo[4,5-f]quinoxaline (DiMeIQx) by between 30 and 50% compared with the control. Fresh-made olive oil, which contained a high amount of dihydroxyphenylethanol derivs., inhibited HA formation more than a 1-yr-old oil did. The inhibition of HA formation was also verified using phenolic compds. extracted from VOO.

IT 31773-95-2, Oleuropein aglycon

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

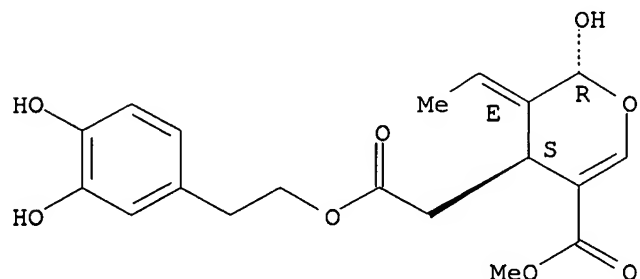
(characterization of, in virgin olive oil and effect on formation of **carcinogenic**/mutagenic heterocyclic amines in a model system)

RN 31773-95-2 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-3,4-dihydro-2-hydroxy-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2R,3E,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:155024 CAPLUS

DOCUMENT NUMBER: 134:310130

TITLE: Olive-oil consumption and health: the possible role of antioxidants

AUTHOR(S): Owen, Robert W.; Giacosa, Attilio; Hull, William E.; Haubner, Roswitha; Wurtele, Gerd; Spiegelhalter, Bertold; Bartsch, Helmut

CORPORATE SOURCE: Division of Toxicology and Cancer Risk Factors, German Cancer Research Center, Heidelberg, D-69120, Germany

SOURCE: Lancet Oncology (2000), 1(Oct.), 107-112  
CODEN: LOANBN; ISSN: 1470-2045

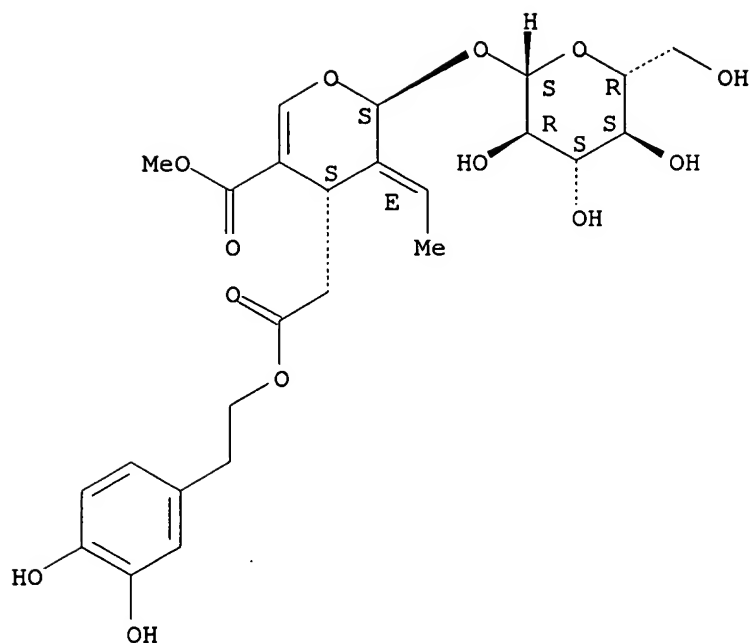
10/712423

PUBLISHER: Lancet Publishing Group  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

- AB A review with 35 refs. In the Mediterranean basin, olive oil, along with fruits, vegetables, and fish, is an important constituent of the diet, and is considered a major factor in preserving a healthy and relatively disease-free population. Epidemiol. data show that the Mediterranean diet has significant protective effects against **cancer** and coronary heart disease. We present evidence that it is the unique profile of the phenolic fraction, along with high intakes of squalene and the monounsaturated fatty acid, oleic acid, which confer its health-promoting properties. The major phenolic compounds identified and quantified in olive oil belong to three different classes: simple phenols (hydroxytyrosol, tyrosol); secoiridoids (oleuropein, the aglycon of ligstroside, and their respective decarboxylated dialdehyde derivatives); and the lignans [(+)-1-acetoxypinoresinol and (+)-pinoresinol]. All three classes have potent antioxidant properties. High consumption of extra-virgin olive oils, which are particularly rich in these phenolic antioxidants (as well as squalene and oleic acid), should afford considerable protection against **cancer** (colon, breast, skin), coronary heart disease, and ageing by inhibiting oxidative stress.
- IT **32619-42-4, Oleuropein**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(Olive-oil consumption and health in relation to the possible role of antioxidants)
- RN 32619-42-4 CAPLUS
- CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.





REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:906581 CAPLUS

DOCUMENT NUMBER: 134:146898

TITLE: Oleuropein, an antioxidant polyphenol from olive oil, is poorly absorbed from isolated perfused rat intestine

AUTHOR(S): Edgecombe, Steven C.; Stretch, Graham L.; Hayball, Peter J.

CORPORATE SOURCE: Centre for Pharmaceutical Research, University of South Australia, Adelaide, 5000, Australia

SOURCE: Journal of Nutrition (2000), 130(12), 2996-3002

CODEN: JONUAI; ISSN: 0022-3166

PUBLISHER: American Society for Nutritional Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Epidemiol. studies have shown that the incidence of heart disease and certain **cancers** is lower in the Mediterranean region. This has been attributed to the high consumption of olive oil in the Mediterranean diet, which contains polyphenolic compds. with antioxidant activity. Although many in vitro studies have been performed to elucidate mechanisms by which these compds. may act, there are virtually no data relating to their fate after ingestion. Therefore, we decided to investigate the intestinal absorption of one of the major olive oil polyphenolics, oleuropein. To do this, a novel in situ intestinal perfusion technique was developed, and the absorption of oleuropein was studied under both iso-osmotic and hypotonic luminal conditions. Oleuropein was absorbed, with an apparent permeability coefficient (Papp) of  $1.47 \pm 0.13 \times 10^{-6}$  cm/s ( $\pm$ SE) observed under iso-osmotic conditions. The mechanism of absorption is unclear but may involve transcellular transport (SGLT1)

or paracellular movement. Under hypotonic conditions, the permeability of oleuropein was significantly greater ( $5.92 \pm 0.49 + 10^{-6}$  cm/s,  $P < 0.001$ ). This increase is thought to be due to an increase in paracellular movement facilitated by the opening of paracellular junctions in response to hypotonicity. Overall, we determined that the olive oil polyphenolic oleuropein can be absorbed, albeit poorly, from isolated perfused rat intestine. Therefore, it is possible that it or its metabolites may confer a pos. health benefit after the consumption of olive oil, most likely via an antioxidant mechanism.

IT 32619-42-4, Oleuropein

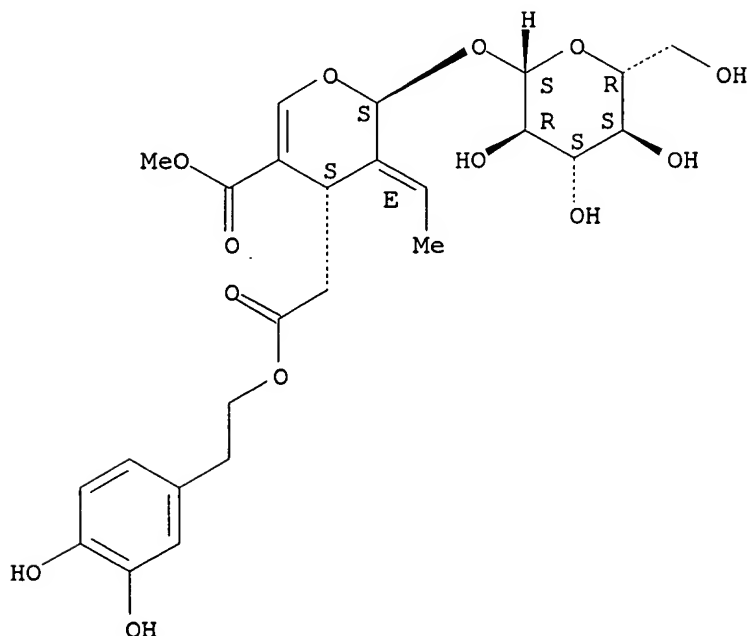
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(oleuropein, an antioxidant polyphenol from olive oil, is poorly absorbed from isolated perfused rat intestine)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:507306 CAPLUS

DOCUMENT NUMBER: 133:207042

TITLE: Phenolic compounds and squalene in olive oils: the concentration and antioxidant potential of total phenols, simple phenols, secoiridoids, lignans and

AUTHOR(S): squalene  
 Owen, R. W.; Mier, W.; Giacosa, A.; Hull, W. E.;  
 Spiegelhalder, B.; Bartsch, H.  
 CORPORATE SOURCE: Division of Toxicology and Cancer Risk Factors,  
 German Cancer Research Center, Heidelberg, Germany  
 SOURCE: Food and Chemical Toxicology (2000), 38(8),  
 647-659  
 CODEN: FCTOD7; ISSN: 0278-6915  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The aim of this study was to evaluate the phenolic antioxidant and squalene content in a range of olive and seed oils. A mean of  $290 \pm 38$  (SEM) mg squalene/100 g was detected. However, while there was a weak significant difference between extra virgin ( $424 \pm 21$  mg/kg) and refined virgin ( $340 \pm 31$  mg/100 g) olive oils, highly significant differences were evident between extra virgin olive oils refined virgin olive oils and seed oils ( $24 \pm 5$  mg/100 g). While seed oils were devoid, on average, the olive oils contained  $196 \pm 19$  mg/kg total phenolics as judged by HPLC anal., but the value for extra virgin ( $232 \pm 15$  mg/kg) was significantly higher than that of refined virgin olive oil ( $62 \pm 12$  mg/kg). Appreciable quantities of simple phenols (hydroxytyrosol and tyrosol) were detected in olive oils, with significant differences between extra virgin ( $41.87 \pm 6.17$ ) and refined virgin olive oils ( $4.72 \pm 215$ ). The major linked phenols were secoiridoids and lignans. Although extra virgin contained higher concns. of secoiridoids ( $27.72 \pm 6.84$ ) than refined olive oils ( $9.30 \pm 3.81$ ) this difference was not significant. On the other hand, the concentration of lignans was significantly higher in extra virgin ( $41.53 \pm 3.93$ ) compared to refined virgin olive oils ( $7.29 \pm 2.56$ ). All classes of phenolics were shown to be potent antioxidants. In future epidemiol. studies, both the nature and source of olive oil consumed should be differentiated in ascertaining cancer risk.

IT 31773-95-2, Oleuropein aglycone 32619-42-4,  
 Oleuropein

RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)

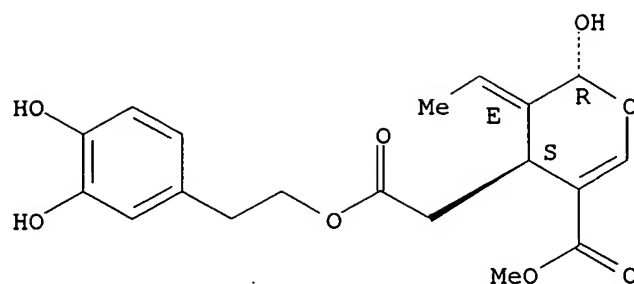
(phenolic compds. and squalene in olive oils, concentration and antioxidant potential of total phenols, simple phenols, secoiridoids, lignans and squalene)

RN 31773-95-2 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-3,4-dihydro-2-hydroxy-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2R,3E,4S)-(9CI) (CA INDEX NAME)

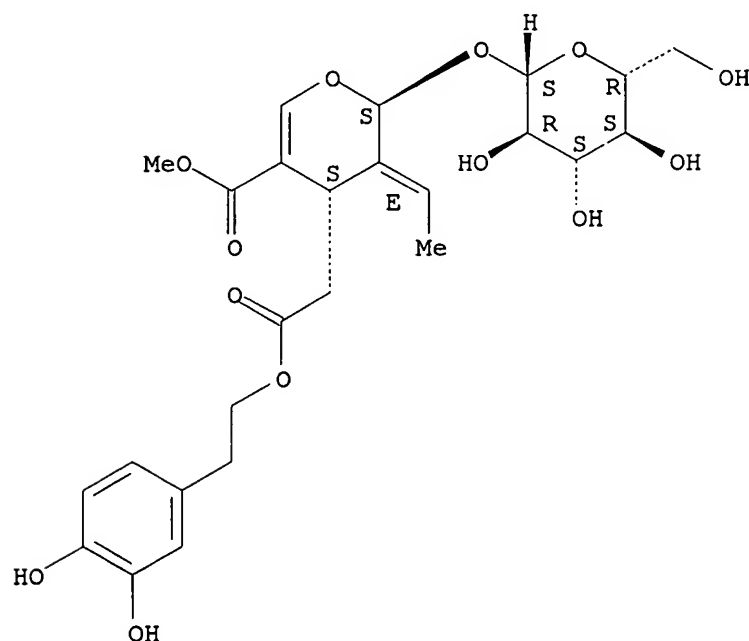
Absolute stereochemistry.  
 Double bond geometry as shown.

10/712423



RN 32619-42-4 CAPLUS  
CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-  
3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester,  
(2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE  
RE FORMAT

L7 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2000:487644 CAPLUS  
DOCUMENT NUMBER: 133:192309  
TITLE: Identification of lignans as major components in  
the phenolic fraction of olive oil  
AUTHOR(S): Owen, Robert W.; Mier, Walter; Giacosa, Attilio;  
Hull, William E.; Spiegelhalter, Bertold; Bartsch,  
Helmut

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Division of Toxicology and Cancer Risk Factors,  
German Cancer Research Center, Heidelberg,  
D-69120, Germany

SOURCE: Clinical Chemistry (Washington, D. C.) (2000),  
46(7), 976-988  
CODEN: CLCHAU; ISSN: 0009-9147

PUBLISHER: American Association for Clinical Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The major phenolic antioxidants in extra virgin olive oil were isolated and purified. Structural anal. was conducted using several spectroscopic techniques, including mass spectrometry and NMR. In particular, detailed <sup>1</sup>H and <sup>13</sup>C NMR data are presented, and several assignment errors in the literature are corrected. The lignans (+)-1-acetoxypinoresinol and (+)-pinoresinol are major components of the phenolic fraction of olive oils. These lignans, which are potent antioxidants, are absent in seed oils and absent in refined virgin oils, but are present at concns. of up to 100 mg/kg (mean ± SE, 41.53 ± 3.93 mg/kg; range, 0.65-99.97 mg/kg) in extra virgin oils. As with the simple phenols and secoiridoids, there is considerable interoil variation in lignan concns. Foods containing high amts. of lignan precursors have been found to be protective against breast, colon, and prostate cancer. Lignans, as natural components of the diet, may be important modulators of cancer chemopreventive activity.

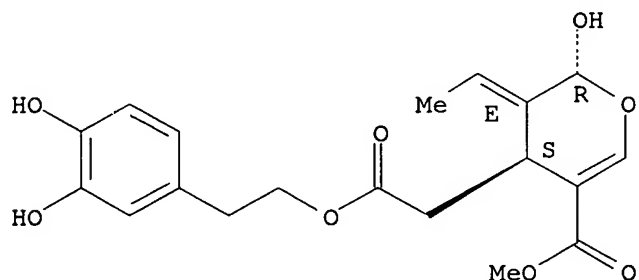
IT 31773-95-2 32619-42-4, Oleuropein  
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lignan components in the phenolic fraction of olive oil)

RN 31773-95-2 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-3,4-dihydro-2-hydroxy-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2R,3E,4S)-(9CI) (CA INDEX NAME)

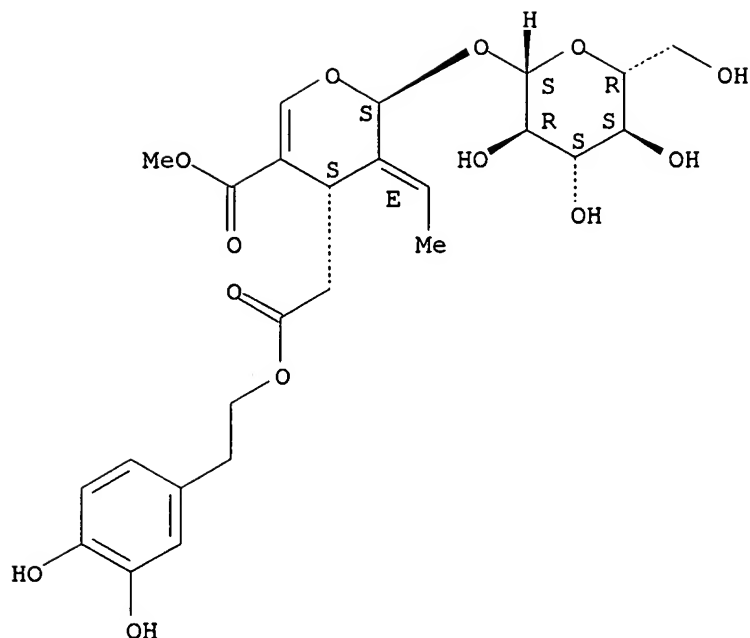
Absolute stereochemistry.  
Double bond geometry as shown.



RN 32619-42-4. CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-(β-D-glucopyranosyloxy)-3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2S,3E,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:454807 CAPLUS

DOCUMENT NUMBER: 133:344249

TITLE: The antioxidant/**anticancer** potential of phenolic compounds isolated from olive oil

AUTHOR(S): Owen, R. W.; Giacosa, A.; Hull, W. E.; Haubner, R.; Spiegelhalder, B.; Bartsch, H.

CORPORATE SOURCE: Division of Toxicology and Cancer Risk Factors, German Cancer Research Centre, Heidelberg, D-69120, Germany

SOURCE: European Journal of Cancer (2000), 36(10), 1235-1247

CODEN: EJCAEL; ISSN: 0959-8049

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In our ongoing studies on the chemoprevention of **cancer** we have a particular interest in the health benefits of the Mediterranean diet, of which olive oil is a major component. Recent studies have shown that extravirgin olive oil contains an abundance of phenolic antioxidants including simple phenols (hydroxytyrosol, tyrosol), aldehydic secoiridoids, flavonoids and lignans (acetoxypinoresinol, pinoresinol). All of these phenolic substances are potent inhibitors of reactive oxygen species attack on, e.g., salicylic acid, 2-deoxyguanosine. Currently there is growing evidence that reactive oxygen species are involved in the etiol. of fat-related **neoplasms** such as **cancer** of the breast and colorectum. A plausible mechanism is a high intake of  $\omega$ -6 polyunsatd. fatty acids which are especially prone to lipid peroxidn. initiated and propagated by reactive oxygen species, leading to the formation (via  $\alpha,\beta$ -unsatd. aldehydes such as

trans-4-hydroxy-2-nonenal) of highly pro-mutagenic exocyclic DNA adducts. Previous studies have shown that the colonic mucosa of **cancer** patients and those suffering from predisposing inflammatory conditions such as ulcerative colitis and Crohn's disease generates appreciably higher quantities of reactive oxygen species compared with normal tissue. We have extended these studies by developing accurate high performance liquid chromatog. (HPLC) methods for the quantitation of reactive oxygen species generated by the fecal matrix. The data shows that the fecal matrix supports the generation of reactive oxygen species in abundance. As yet, there is a dearth of evidence linking this capacity to actual components of the diet which may influence the colorectal milieu. However, using the newly developed methodol. we can demonstrate that the antioxidant phenolic compds. present in olive oil are potent inhibitors of free radical generation by the fecal matrix. This indicates that the study of the inter-relation between reactive oxygen species and dietary antioxidants is an area of great promise for elucidating mechanisms of colorectal **carcinogenesis** and possible future chemopreventive strategies.

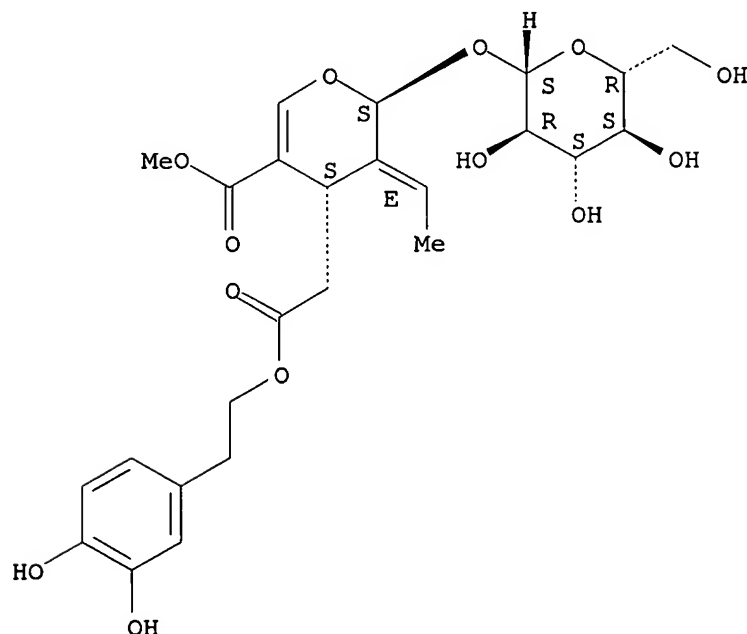
IT 32619-42-4P

RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(antioxidant/**anticancer** potential of phenolic compds. isolated from olive oil)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



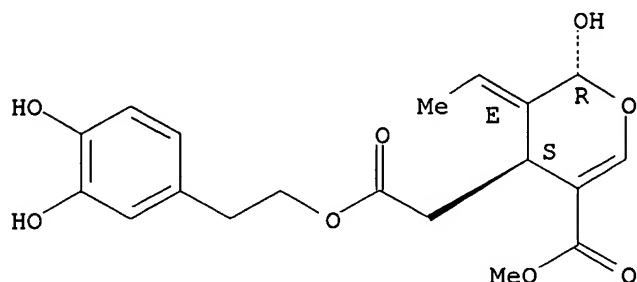
IT 31773-95-2P

RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)

(antioxidant/**anticancer** potential of phenolic compds.  
isolated from olive oil)

RN 31773-95-2 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-3,4-dihydro-2-hydroxy-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2R,3E,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE  
RE FORMAT

L7 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:319686 CAPLUS

DOCUMENT NUMBER: 132:339119

TITLE: Polyphenols: simple structures with high potential

AUTHOR(S): Metz, Gunter

CORPORATE SOURCE: Blaubeuren, 89143, Germany

SOURCE: Pharmazeutische Zeitung (2000), 145(16),  
1273-1275,1278

CODEN: PHZIAP; ISSN: 0031-7136

PUBLISHER: Govi-Verlag Pharmazeutischer Verlag

DOCUMENT TYPE: Journal; General Review

LANGUAGE: German

AB A review with 6 refs. is given on the medicinal effects of polyphenols  
(e.g. **anticarcinogen**, antioxidative) including phenolic  
acids, cumarins and furocumarins, propolis, ingredients in olive oil,  
and ACA.

IT 32619-42-4, Oleuropein

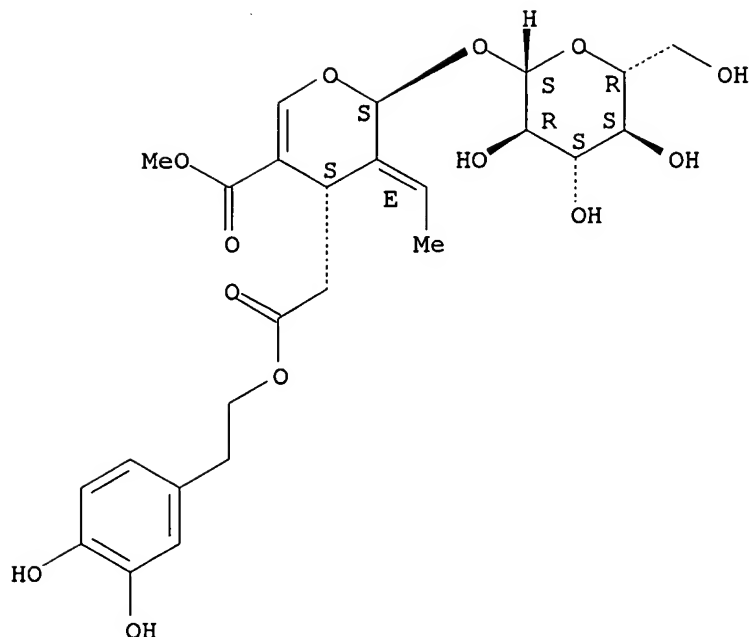
RL: BAC (Biological activity or effector, except adverse); BOC  
(Biological occurrence); BSU (Biological study, unclassified); THU  
(Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES  
(Uses)

(medicinal effects of polyphenols)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-  
3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester,  
(2S,3E,4S)-(9CI) (CA INDEX NAME)Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.





REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:467227 CAPLUS

DOCUMENT NUMBER: 131:226102

TITLE: Studies on constituents with cytotoxic activity from the stem bark of *Syringa velutina*

AUTHOR(S): Park, Hee-Juhn; Lee, Myung-Sun; Lee, Kyung-Tae; Sohn, Il-Cheol; Han, Yong-Nam; Miyamoto, Ken-Ichi  
CORPORATE SOURCE: Department of Botanical Resources, Sangi University, Wonju, 220-702, S. Korea

SOURCE: Chemical & Pharmaceutical Bulletin (1999), 47(7), 1029-1031

CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cytotoxic compds., oleuropein and a phenylethanoid glycoside (I) were isolated from the stem bark of *Syringa velutina* KOM. along with coniferylaldehyde 4-O-glucoside, syringin, ligstroside, (+)-syringaresinol 4-O-glucoside, (+)-medioresinol 4''-O-glucoside and (-)-olivil 4''-O-glucoside. I was identified to be 3,4-dihydroxyphenylethyl alc. 8-O-β-D-glucopyranoside. Alc. 8-O-β-D-glucopyranoside. This compound showed the most potent cytotoxic effect on several tumor cell lines (P-388, L-1210, SNU-5 and HL-60) among eight compds. isolated in the present study. We suggest that the 3,4-dihydroxyphenylethoxy moiety of this compound contributes to cytotoxicity.

IT 32619-42-4, Oleuropein

RL: BAC (Biological activity or effector, except adverse); BOC

10/712423

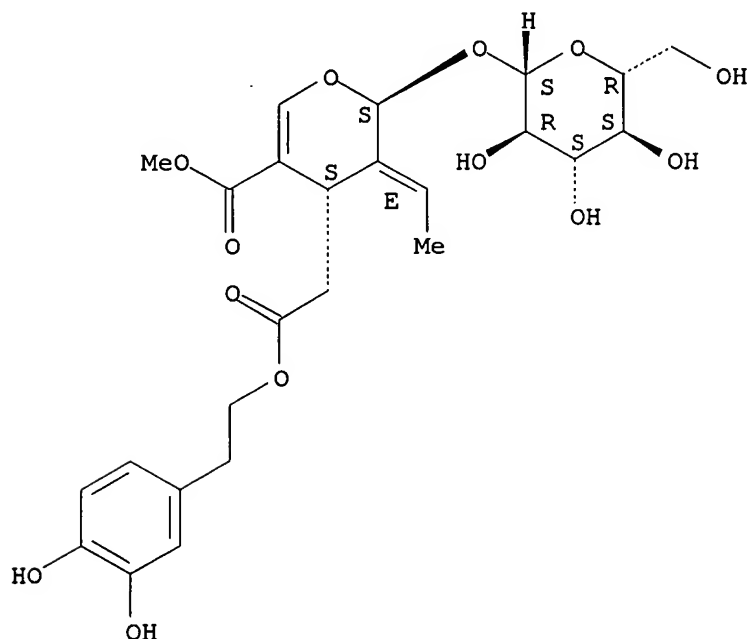
(Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(cytotoxic activities of constituents from stem bark of *Syringa velutina*)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:380086 CAPLUS

DOCUMENT NUMBER: 129:81138

TITLE: Free radical-scavenging properties of olive oil polyphenols

AUTHOR(S): Visioli, Francesco; Bellomo, Giorgio; Galli, Claudio

CORPORATE SOURCE: Institute of Pharmacological Sciences, University of Milan, Italy

SOURCE: Biochemical and Biophysical Research Communications (1998), 247(1), 60-64  
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Plants in the Mediterranean basin, such as vine and olive trees, have developed an array of antioxidant defences to protect themselves from

Searcher : Shears 571-272-2528

environmental stress. Accordingly, the incidence of coronary heart disease and certain **cancers** is lower in the Mediterranean area, where olive oil is the dietary fat of choice. As opposed to other vegetable oils, extra virgin olive oil, which is obtained by phys. pressure from a whole fruit, is rich in phenolic components that are responsible for the particular stability of the oil. We have investigated the scavenging actions of some olive oil phenolics, namely hydroxytyrosol and oleuropein, with respect to superoxide anion generation, neutrophils respiratory burst, and hypochlorous acid. The low EC50s indicate that both compds. are potent scavengers of superoxide radicals and inhibitors of neutrophils respiratory burst: whenever demonstrated in vivo, these properties may partially explain the observed lower incidence of CHD and **cancer** associated with the Mediterranean diet.

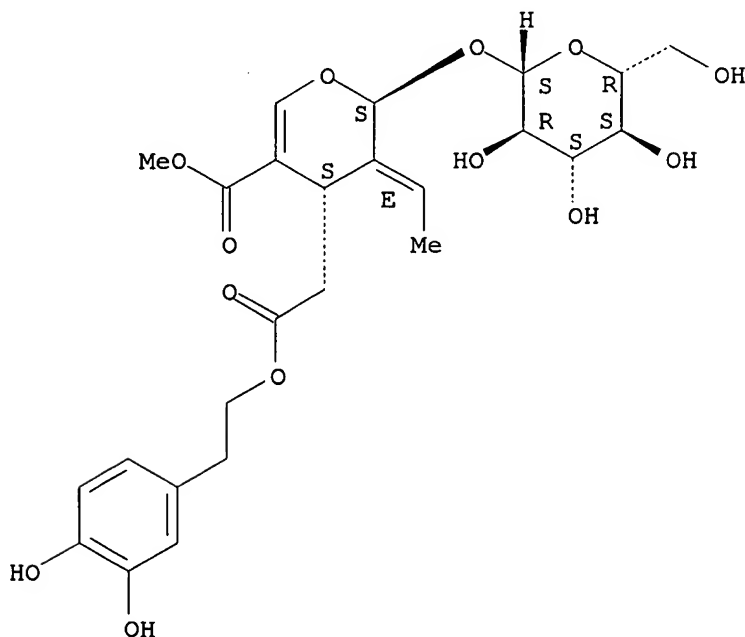
IT 32619-42-4, Oleuropein

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(free radical-scavenging properties of olive oil polyphenols)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-  
3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester,  
(2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1998:20210 CAPLUS  
DOCUMENT NUMBER: 128:162831

Searcher : Shears 571-272-2528

TITLE: Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages

AUTHOR(S): Visioli, Francesco; Bellosta, Stefano; Galli, Claudio

CORPORATE SOURCE: Institute of Pharmacological Sciences, Milan, 20133, Italy

SOURCE: Life Sciences (1998), 62(6), 541-546  
CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

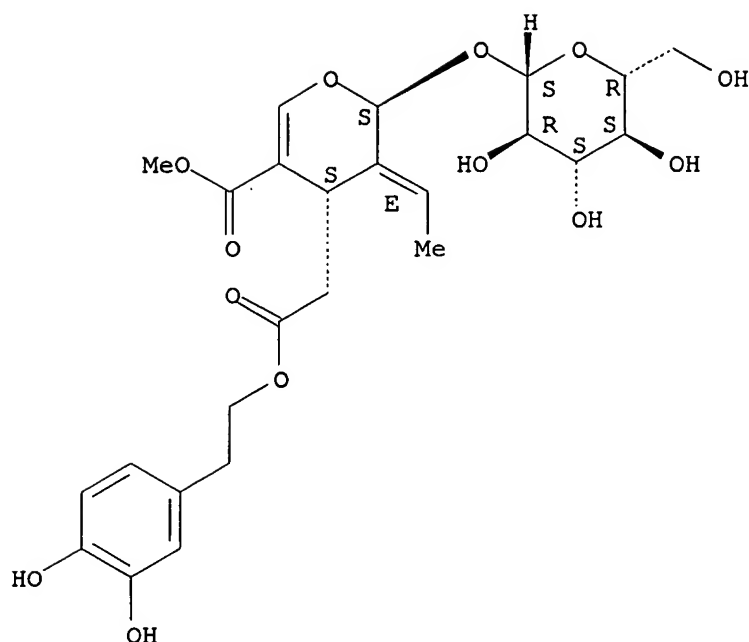
AB The Mediterranean diet, rich in fresh fruits and vegetables, has been associated with a lower incidence of cardiovascular disease and **cancer**, partly because of its high proportion of bioactive compds. such as vitamins, flavonoids and polyphenols. The major lipid component of such diet is the drupe-derived olive oil, that can be distinguished from other seed oils for the peculiar composition of its non-triglyceride fraction. In fact, several minor components, including polyphenols, grant the oil its particular taste and aroma. Oleuropein, the most abundant among these components, has been shown to be a potent antioxidant endowed with antiinflammatory properties. We investigated the effects of oleuropein on NO release in cell culture and its activity toward nitric oxide synthase (iNOS) expression. The results show that oleuropein dose-dependently enhance nitrite production in LPS-challenged mouse macrophages. This effect was blocked by the iNOS inhibitor L-NAME, indicating increased iNOS activity. Also, Western blot anal. of cell homogenates show that oleuropein increases iNOS expression in such cells. Taken together, our data suggest that, during endotoxin challenge, oleuropein potentiates the macrophage-mediated response, resulting in higher NO production, currently believed to be beneficial for cellular and organismal protection.

IT **32619-42-4**, Oleuropein  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oleuropein from olive oil enhances nitric oxide production by macrophages)

RN 32619-42-4 CAPLUS

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester, (2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:519455 CAPLUS

DOCUMENT NUMBER: 122:298024

TITLE: Waste waters from olive oil production are rich in natural antioxidants

AUTHOR(S): Visioli, F.; Vinceri, F. F.; Galli, C.

CORPORATE SOURCE: Inst. Pharmacological Sci., Univ. Milan, Milan, I-20133, Italy

SOURCE: Experientia (1995), 51(1), 32-4

CODEN: EXPEAM; ISSN: 0014-4754

PUBLISHER: Birkhaeuser

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Milling of olive paste during olive oil production is accompanied by continuous washing with water, i.e. malaxation. The resulting wastewater is currently discarded. Since olives and olive oil are rich in natural antioxidants, we hypothesized that some of these might be extracted from the olive paste during malaxation. Interest in natural antioxidants is increasing because of the growing body of evidence indicating the involvement of oxygen-derived free radicals in several pathol. processes, such as cancer and atherosclerosis. A wastewater extract was characterized by HPLC and tested in a model of lipid peroxidn., copper sulfate-induced oxidation of low d. lipoproteins. The results demonstrate that wastewater exts. have powerful antioxidant activity and might therefore represent a cheap, as yet unused, source of antioxidants.

IT 32619-42-4, Oleuropein

RL: MSC (Miscellaneous)

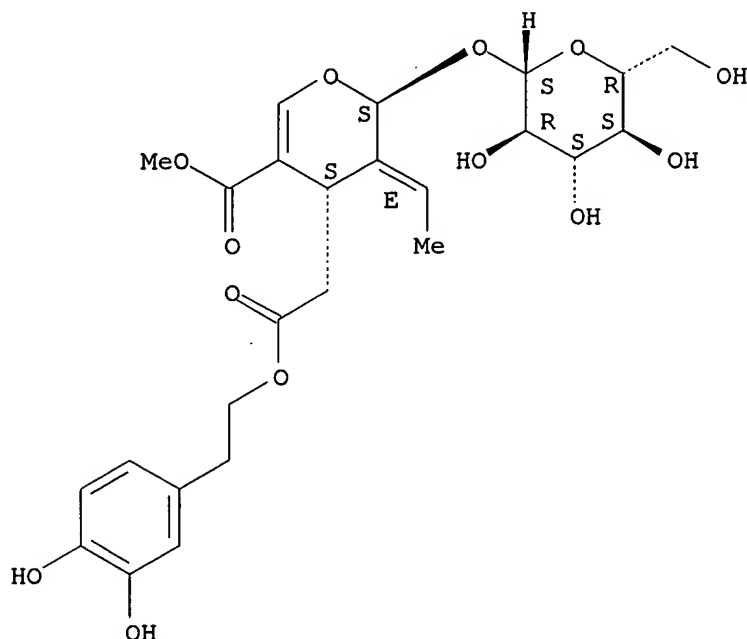
(olive oil manufacturing wastewater antioxidants)

RN 32619-42-4 CAPLUS

10/712423

CN 2H-Pyran-4-acetic acid, 3-ethylidene-2-( $\beta$ -D-glucopyranosyloxy)-  
3,4-dihydro-5-(methoxycarbonyl)-, 2-(3,4-dihydroxyphenyl)ethyl ester,  
(2S,3E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



FILE 'CAOLD' ENTERED AT 12:34:32 ON 03 MAR 2006  
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FILE COVERS 1907-1966  
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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L8 2 L4

L8 ANSWER 1 OF 2 CAOLD COPYRIGHT 2006 ACS on STN  
AN CA64:8124e CAOLD  
TI oleuropein - (III)

Searcher : Shears 571-272-2528

10/712423

AU Panizzi, Luigi; Scarpati, M. L.; Trogolo, C.  
IT 4809-64-7 32619-42-4

L8 ANSWER 2 OF 2 CAOLD COPYRIGHT 2006 ACS on STN  
AN CA57:3398c CAOLD  
TI constitution of oleuropein, a bitter glucoside of the olive with  
hypotensive action - (II)  
AU Panizzi, Luigi; Scarpati, M. L.; Oriente, G.  
IT 4751-57-9 7417-21-2 10597-60-1 32619-42-4 51856-81-6  
90613-43-7 91143-92-9 91556-07-9 91966-89-1 92038-78-3 92157-73-8  
92371-95-4 92730-99-9 92788-48-2 93404-86-5 96536-15-1 96650-87-2

FILE 'USPATFULL' ENTERED AT 12:34:48 ON 03 MAR 2006  
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Mar 2006 (20060302/PD)  
FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)  
HIGHEST GRANTED PATENT NUMBER: US7007305  
HIGHEST APPLICATION PUBLICATION NUMBER: US2006048257  
CA INDEXING IS CURRENT THROUGH 28 Feb 2006 (20060228/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Mar 2006 (20060302/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

L9 74 SEA ABB=ON PLU=ON L4  
L10 27 SEA ABB=ON PLU=ON L9 AND (?CANCER? OR ?CARCIN? OR  
?TUMOUR? OR ?TUMOR? OR ?NEOPLAS?)  
L11 3 SEA ABB=ON PLU=ON L10 NOT (PY=>2002 OR PD=>20021209)

L11 ANSWER 1 OF 3 USPATFULL on STN  
ACCESSION NUMBER: 2001:32806 USPATFULL  
TITLE: Water-soluble extract from olives  
INVENTOR(S): Crea, Roberto, San Mateo, CA, United States  
Caglioti, Luciano, Rome, Italy  
PATENT ASSIGNEE(S): CreAgri L.L.C., Hayward, CA, United States (U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6197308	B1	20010306
APPLICATION INFO.:	US 1999-359150		19990722 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-93818P	19980723 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Lilling, Herbert J.	
LEGAL REPRESENTATIVE:	Dehlinger, Peter J.	
NUMBER OF CLAIMS:	2	
EXEMPLARY CLAIM:	1	
LINE COUNT:	309	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides olive-derived vegetation water substantially  
free of monophenolic compounds (e.g., tyrosol and its derivatives)  
from olive pits. According to one aspect of the invention, the pits  
or seeds are removed from the olives prior to pressing. The pitless  
pulp or meat is then pressed to obtain a liquid-phase mixture  
including olive oil, vegetation water, and solid by-products. The

Searcher : Shears 571-272-2528

10/712423

vegetation water is separated from the rest of the liquid-phase mixture and collected. The vegetation water is useful as a source of oleuropein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2000:174104 USPATFULL  
TITLE: Water-soluble extract from olives  
INVENTOR(S): Crea, Roberto, San Mateo, CA, United States  
Caglioti, Luciano, Rome, Italy  
PATENT ASSIGNEE(S): CreAgri, Inc., Hayward, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6165475		20001226
APPLICATION INFO.:	US 2000-491680		20000126 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1999-359150, filed on 22 Jul 1999		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-93818P	19980723 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Lilling, Herbert J.	
LEGAL REPRESENTATIVE:	Dehlinger, Peter J.	
NUMBER OF CLAIMS:	7	
EXEMPLARY CLAIM:	1	
LINE COUNT:	345	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides a stable, olive-derived vegetation water substantially free of monophenolic compounds (e.g., tyrosol and its derivatives). The olive or seeds are removed from the olives prior to pressing. The pitless pulp or meat is then pressed to obtain a liquid-phase mixture including olive oil, vegetation water, and solid by-products. The vegetation water is separated from the rest of the liquid-phase mixture and collected, and stabilized for long term storage by acidification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 3 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2000:153273 USPATFULL  
TITLE: Use of an extract from the leaves of Olea Europea as an antiradical  
INVENTOR(S): Amari, Giorgio, Milan, Italy  
PATENT ASSIGNEE(S): B & T S.r.l., Milan, Italy (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6146637		20001114
APPLICATION INFO.:	US 1999-250163		19990216 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1998-MI317	19980219
DOCUMENT TYPE:	Utility	

Searcher : Shears 571-272-2528



FILE SEGMENT: Granted  
PRIMARY EXAMINER: Lilling, Herbert J.  
LEGAL REPRESENTATIVE: Young & Thompson  
NUMBER OF CLAIMS: 2  
EXEMPLARY CLAIM: 1  
LINE COUNT: 152

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of an extract from the leaves of *Olea Europea* as an antiradical. Preferably, the extract is added to a preparation wherein the concentration of the extract does not exceed 0.5% by weight. The extract can be used both for preparing cosmetic products, such as cosmetic creams--particularly sun protection creams--and for preparing alimentary products--particularly dietetic products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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FILE 'EMBASE' ENTERED AT 12:36:35 ON 03 MAR 2006  
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L12 406 SEA ABB=ON PLU=ON L4  
L13 50 SEA ABB=ON PLU=ON L12 AND (CANCER? OR CARCIN? OR TUMOUR?  
OR TUMOR? OR NEOPLAS? OR ANTICANCER? OR ANTICARCIN? OR  
ANTITUMOUR? OR ANTITUMOR? OR ANTINEOPLAS?)  
L14 35 DUP REM L13 (15 DUPLICATES REMOVED)

L14 ANSWER 1 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2005:329527 BIOSIS  
DOCUMENT NUMBER: PREV200510114940  
TITLE: Quantitation of oleuropein and related metabolites in decoctions of *Olea europaea* leaves from ten Greek cultivated varieties by HPLC with diode array detection (HPLC-DAD).  
AUTHOR(S): Agalias, Apostolis; Melliou, Eleni; Magiatis, Prokopios; Mitaku, Sofia [Reprint Author]; Gikas, Evangelos; Tsarbopoulos, Anthony  
CORPORATE SOURCE: Univ Athens, Dept Pharm, Div Pharmacognosy and Nat Prod Chem, Panepistimiopolis Zografou, GR-15771 Athens, Greece  
mitakou@pharm.uoa.gr  
SOURCE: Journal of Liquid Chromatography & Related Technologies, (2005) Vol. 28, No. 10, pp. 1557-1571.  
ISSN: 1082-6076.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 25 Aug 2005  
Last Updated on STN: 25 Aug 2005

AB An extraction procedure and chromatographic methodology for the simultaneous quantitation of four major constituents in the boiling water extracts (decoctions) of *Olea europaea* leaves has been developed. The four studied constituents were oleuropein, elenolic acid, hydroxytyrosol, and tyrosol. The quantitation was performed using HPLC-DAD, whereas qualitative data were acquired using LC-MS.

The developed methodology was applied in the study of ten Olea europaea varieties commonly cultivated in Greece. The chromatographic analysis revealed important differences among the varieties. The decoction of variety gaidouroelia was identified as the best source of oleuropein, but it was completely lacking of elenolic acid. The decoction of variety koronaiiki was the best source of hydroxytyrosol, whereas the variety mastoides was the best source of tyrosol and elenolic acid. In addition, the methanol and acetone extracts of one of the studied varieties (koronaiiki) were investigated, in order to compare the concentration of oleuropein in the extracts and the decoction. Interestingly, only a very low percent of the total oleuropein is present in the traditionally prepared decoction, while elenolic acid, which is a minor constituent of the extracts, was found to be one of the major constituents of the decoction.

L14 ANSWER 2 OF 35 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN  
 ACCESSION NUMBER: 2005486238 EMBASE  
 TITLE: Astonishing diversity of natural surfactants: 5. Biologically active glycosides of aromatic metabolites.  
 AUTHOR: Dembitsky V.M.  
 CORPORATE SOURCE: V.M. Dembitsky, Department of Organic Chemistry, Hebrew University, P.O. Box 39231, Jerusalem 91391, Israel. dvalery@cc.huji.ac.il  
 SOURCE: Lipids, (2005) Vol. 40, No. 9, pp. 869-900. . Refs: 328  
 ISSN: 0024-4201 CODEN: LPDSAP  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20051128  
 Last Updated on STN: 20051128  
 AB This review article presents 342 aromatic glycosides, isolated from and identified in plants and microorganisms, that demonstrate different biological activities. They are of great interest, especially for the medicinal and/or pharmaceutical industries. These biologically active natural surfactants are good prospects for the future chemical preparation of compounds useful as antioxidant, **anticancer**, antimicrobial, and antibacterial agents. These glycosidic compounds have been classified into several groups, including simple aromatic compounds, stilbenes, phenylethanoids, phenylpropanoids, naphthalene derivatives, and anthracene derivatives. Copyright .COPYRGT. 2005 by AOCs Press.

L14 ANSWER 3 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 1  
 ACCESSION NUMBER: 2005:465993 BIOSIS  
 DOCUMENT NUMBER: PREV200510246592  
 TITLE: Oleuropein, a non-toxic olive iridoid, is an anti-tumor agent and cytoskeleton disruptor.  
 AUTHOR(S): Hamdi, Hamdi K. [Reprint Author]; Castellon, Raquel  
 CORPORATE SOURCE: H2RC Corp, 1920 E Katella Ave, Suite U, Orange, CA 92867 USA  
 hkhamdi@mail.com  
 SOURCE: Biochemical and Biophysical Research Communications, (SEP 2 2005) Vol. 334, No. 3, pp. 769-778.

10/712423

CODEN: BBRCA9. ISSN: 0006-291X.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 9 Nov 2005  
Last Updated on STN: 9 Nov 2005

AB Oleuropein, a non-toxic secoiridoid derived from the olive tree, is a powerful antioxidant and anti-angiogenic agent. Here, we show it to be a potent anti-cancer compound, directly disrupting actin filaments in cells and in a cell-free assay. Oleuropein inhibited the proliferation and migration of advanced-grade human tumor cell lines in a dose-responsive manner. In a novel tube-disruption assay. Oleuropein irreversibly rounded cancer cells, preventing their replication, motility, and invasiveness; these effects were reversible in normal cells. When administered orally to mice that developed spontaneous tumors, Oleuropein completely regressed tumors in 9-12 days. When tumors were resected prior to complete regression, they lacked cohesiveness and had a crumbly consistency. No viable cells could be recovered from these tumors. These observations elevate Oleuropein from a non-toxic antioxidant into a potent anti-tumor agent with direct effects against tumor cells. Our data may also explain the cancer-protective effects of the olive-rich Mediterranean diet. (c) 2005 Elsevier Inc. All rights reserved.

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ACCESSION NUMBER: 2005131586 EMBASE  
TITLE: Differential anti-inflammatory effects of phenolic compounds from extra virgin olive oil identified in human whole blood cultures.  
AUTHOR: Miles E.A.; Zoubouli P.; Calder P.C.  
CORPORATE SOURCE: Dr. E.A. Miles, Institute of Human Nutrition, School of Medicine, University of Southampton, Southampton, United Kingdom. eam@soton.ac.uk.  
SOURCE: Nutrition, (2005) Vol. 21, No. 3, pp. 389-394. .  
Refs: 28  
ISSN: 0899-9007 CODEN: NUTRER  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20050407  
Last Updated on STN: 20050407

AB Objective: The olive oil-rich Mediterranean diet protects against cardiovascular disease, which involves inflammatory processes. This study investigated the effects of phenolic compounds found in extra virgin olive oil on inflammatory mediator production by human mononuclear cells. Methods: Diluted human blood cultures were stimulated with lipopolysaccharide in the presence of phenolics (vanillic, p-coumaric, syringic, homovanillic and caffeic acids, kaempferol, oleuropein glycoside, and tyrosol) at concentrations of 10<sup>-7</sup> to 10<sup>-4</sup> M. Concentrations of the inflammatory cytokines tumor necrosis factor- $\alpha$ , interleukin-1 $\beta$ , and interleukin-6 and of the inflammatory eicosanoid prostaglandin E(2) were measured by enzyme-linked immunosorbent assay. Results: Oleuropein glycoside and caffeic acid decreased the concentration of

interleukin-1 $\beta$ . At a concentration of 10(-4) M, oleuropein glycoside inhibited interleukin-1 $\beta$  production by 80%, whereas caffeic acid inhibited production by 40%. Kaempferol decreased the concentration of prostaglandin E(2). At a concentration of 10 (-4) M, kaempferol inhibited prostaglandin E(2) production by 95%. No effects were seen on concentrations of interleukin-6 or **tumor** necrosis factor- $\alpha$  and there were no effects of the other phenolic compounds. Conclusions: Some, but not all, phenolic compounds derived from extra virgin olive oil decrease inflammatory mediator production by human whole blood cultures. This may contribute to the antiatherogenic properties ascribed to extra virgin olive oil. .COPYRGT. 2005 Elsevier Inc. All rights reserved.

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STN DUPLICATE 2

ACCESSION NUMBER: 2005:330331 BIOSIS  
DOCUMENT NUMBER: PREV200510116584  
TITLE: The phenolic compounds of olive oil: structure, biological activity and beneficial effects on human health.  
AUTHOR(S): Tripoli, Elisa; Giammanco, Marco [Reprint Author]; Tabacchi, Garden; Di Majo, Danila; Giammanco, Santo; La Guardia, Maurizio  
CORPORATE SOURCE: Univ Palermo, Fac Pharm, Inst Physiol and Human Nutr, Via Augusto Elia 3, I-90127 Palermo, Italy  
giammanco@unipa.it  
SOURCE: Nutrition Research Reviews, (JUN 2005) Vol. 18, No. 1, pp. 98-112.  
CODEN: NREREX. ISSN: 0954-4224.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 25 Aug 2005  
Last Updated on STN: 25 Aug 2005

AB The Mediterranean diet is rich in vegetables, cereals, fruit, fish, milk, wine and olive oil and has salutary biological functions. Epidemiological studies have shown a lower incidence of atherosclerosis, cardiovascular diseases and certain kinds of **cancer** in the Mediterranean area. Olive oil is the main source of fat, and the Mediterranean diet's healthy effects can in particular be attributed not only to the high relationship between unsaturated and saturated fatty acids in olive oil but also to the antioxidant property of its phenolic compounds. The main phenolic compounds, hydroxytyrosol and oleuropein, which give extra-virgin olive oil its bitter, pungent taste, have powerful antioxidant activity both in vivo and in vitro. The present review focuses on recent works analysing the relationship between the structure of olive oil polyphenolic compounds and their antioxidant activity. These compounds' possible beneficial effects are due to their antioxidant activity, which is related to the development of atherosclerosis and **cancer**, and to anti-inflammatory and antimicrobial activity.

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ACCESSION NUMBER: 2005079028 EMBASE  
TITLE: The antioxidant properties of Greek foods and the flavonoid content of the Mediterranean menu.  
AUTHOR: Vasilopoulou E.; Georga K.; Joergensen M.B.; Naska A.; Trichopoulou A.  
CORPORATE SOURCE: A. Trichopoulou, Department of Hygiene/Epidemiology,

School of Medicine, Natl./Kapodistrian Univ. of Athens,  
Mikras Asias 75, Athens 115 27, Greece.  
antonia@nut.uoa.gr

SOURCE: Current Medicinal Chemistry: Immunology, Endocrine and  
Metabolic Agents, (2005) Vol. 5, No. 1, pp. 33-45. .  
Refs: 117  
ISSN: 1568-0134 CODEN: CMCIC8

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer  
017 Public Health, Social Medicine and Epidemiology  
018 Cardiovascular Diseases and Cardiovascular  
Surgery  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20050303  
Last Updated on STN: 20050303

AB The Mediterranean diet is currently attracting interest because of its health benefits that may be due, in part, to the high content of this diet in antioxidant phytochemicals. The variety and amount of phytochemicals taken with the consumption of primary and composite foods of the Mediterranean diet may provide better antiatherogenic properties than single phytochemicals. Flavonoids are the most important group of plant antioxidants. The Mediterranean diet is characterized by high intake of olive oil, fruit, vegetables, cereals, and legumes, some of which are good sources of flavonoids. Flavonoids consist of six principal classes: flavones, flavonols, flavan-3-ols, flavanones, anthocyanidins and isoflavones. The flavonoid intake from a traditional Greek plant-based weekly menu was calculated and the daily average flavonoid intake was found 118.6 mg/d, of which flavanones contribute 32% (38.5 mg/d), catechins (the most important group of flavan-3-ols) contribute 28% (32.7 mg/d), flavonols 22% (26.4 mg/d), anthocyanidins 9% (11 mg/d), flavones 8% (8.7 mg/d) and isoflavones contribute 1% (1.3 mg/d). Herbs and spices, which are commonly used in the traditional Greek cuisine, although added in small quantities, significantly contribute to the flavonol and flavone intake due to frequent consumption. The Greek version of the Mediterranean diet with its high consumption of fruit and vegetables is characterized by high intake of flavonoids in comparison to diets in northern European countries. .COPYRG. 2005 Bentham Science Publishers Ltd.

L14 ANSWER 7 OF 35 MEDLINE on STN

ACCESSION NUMBER: 2004559974 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15487893

TITLE: Acid-induced structural modifications of unsaturated  
Fatty acids and phenolic olive oil constituents by  
nitrite ions: a chemical assessment.

AUTHOR: Napolitano Alessandra; Panzella Lucia; Savarese Maria;  
Sacchi Raffaele; Giudicianni Italo; Paolillo Livio;  
d'Ischia Marco

CORPORATE SOURCE: Department of Organic Chemistry and Biochemistry,  
University of Naples Federico II, Via Cinthia 4,  
I-80126 Naples, Italy.. alesnapo@unina.it

SOURCE: Chemical research in toxicology, (2004 Oct) Vol. 17,  
No. 10, pp. 1329-37.

10/712423

JOURNAL code: 8807448. ISSN: 0893-228X.  
PUB. COUNTRY: United States.  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200503  
ENTRY DATE: Entered STN: 20041110  
Last Updated on STN: 20050330  
Entered Medline: 20050329

AB The structural modifications of the unsaturated fatty acid components of triglycerides in extra virgin olive oil (EVOO) following exposure to nitrite ions in acidic media were determined by two-dimensional (2D) NMR spectroscopy, aided by (15)N labeling and GC analysis, allowing investigation of the matrix without fractionation steps. In the presence of excess nitrite ions in a 1% sulfuric acid/oil biphasic system, extensive double bond isomerization of the oleic/linoleic acid components of triglycerides was observed associated with nitration/oxidation processes. Structurally modified species were identified as E/Z-nitroalkene, 1,2-nitrohydroxy, and 3-nitro-1-alkene(1,5-diene) derivatives based on (1)H, (13)C, and (15)N 2D NMR analysis in comparison with model compounds. Minor constituents of EVOO, including phenolic compounds and tocopherols, were also substantially modified by nitrite-derived nitrating species, even under milder reaction conditions relevant to those occurring in the gastric compartments. Novel nitrated derivatives of tyrosol, hydroxytyrosol, and oleuropein (6-8) were identified by LC/MS analysis of the polar fraction of EVOO and by comparison with synthetic samples. Overall, these results provide the first systematic description at the chemical level of the consequences of exposing EVOO to nitrite ions at acidic pH and offer an improved basis for further investigations in the field of toxic nitrosation/nitration reactions and dietary antinitrosating agents.

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ACCESSION NUMBER: 2005049849 EMBASE  
TITLE: Olive oil and modulation of cell signaling in disease prevention.  
AUTHOR: Wahle K.W.J.; Caruso D.; Ochoa J.J.; Quiles J.L.  
CORPORATE SOURCE: K.W.J. Wahle, School of Life Sciences, Robert Gordon University, Aberdeen, AB25 1HG, United Kingdom.  
k.wahle-1@rgu.ac.uk  
SOURCE: Lipids, (2004) Vol. 39, No. 12, pp. 1223-1231. .  
Refs: 86  
ISSN: 0024-4201 CODEN: LPDSAP  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20050210  
Last Updated on STN: 20050210

AB Epidemiological studies show that populations consuming a predominantly plant-based Mediterranean-style diet exhibit lower incidences of chronic diseases than those eating a northern European or North American diet. This observation has been attributed to the greater consumption of fruits and vegetables and the lower consumption

of animal products, particularly fat. Although total fat intake in Mediterranean populations can be higher than in other regions (ca. 40% of calories), the greater proportion is derived from olive oil and not animals. Increased olive oil consumption is implicated in a reduction in cardiovascular disease, rheumatoid arthritis, and, to a lesser extent, a variety of **cancers**. Olive oil intake also has been shown to modulate immune function, particularly the inflammatory processes associated with the immune system. Olive oil is a nonoxidative dietary component, and the attenuation of the inflammatory process it elicits could explain its beneficial effects on disease risk since oxidative and inflammatory stresses appear to be underlying factors in the etiology of these diseases in man. The antioxidant effects of olive oil are probably due to a combination of its high oleic acid content (low oxidation potential compared with linoleic acid) and its content of a variety of plant antioxidants, particularly oleuropein, hydroxytyrosol, and tyrosol. It is also possible that the high oleic acid content and a proportionate reduction in linoleic acid intake would allow a greater conversion of  $\alpha$ -linolenic acid (18:3n-3) to longer-chain n-3 PUFA, which have characteristic health benefits. Adoption of a Mediterranean diet could confer health benefits in high-risk populations.

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STN DUPLICATE 3

ACCESSION NUMBER: 2004:114714 BIOSIS  
DOCUMENT NUMBER: PREV200400104817  
TITLE: Herbal bioactivation: The good, the bad and the ugly.  
AUTHOR(S): Zhou, Shufeng [Reprint Author]; Koh, Hwee-Ling; Gao, Yihuai; Gong, Zhi-yuan; Lee, Edmund Jon Deoon  
CORPORATE SOURCE: Department of Pharmacy, Faculty of Science, National University of Singapore, 18 Science Drive 4, Singapore, 117543, Singapore  
phazsf@nus.edu.sg  
SOURCE: Life Sciences, (January 9 2004) Vol. 74, No. 8, pp. 935-968. print.  
ISSN: 0024-3205 (ISSN print).  
DOCUMENT TYPE: Article  
General Review; (Literature Review)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 25 Feb 2004  
Last Updated on STN: 25 Feb 2004

AB It has been well established that the formation of reactive metabolites of drugs is associated with drug toxicity. Similarly, there are accumulating data suggesting the role of the formation of reactive metabolites/intermediates through bioactivation in herbal toxicity and **carcinogenicity**. It has been hypothesized that the resultant reactive metabolites following herbal bioactivation covalently bind to cellular proteins and DNA, leading to toxicity via multiple mechanisms such as direct cytotoxicity, oncogene activation, and hypersensitivity reactions. This is exemplified by aristolochic acids present in *Aristolochia* spp, undergoing reduction of the nitro group by hepatic cytochrome P450 (CYP1A1/2) or peroxidases in extrahepatic tissues to reactive cyclic nitrenium ion. The latter was capable of reacting with DNA and proteins, resulting in activation of H-ras oncogene, gene mutation and finally **carcinogenesis**. Other examples are pulegone present in essential oils from many mint species; and teucrin A, a diterpenoid found in germander (*Teucrium chamaedrys*) used as an adjuvant to slimming diets. Extensive pulegone metabolism generated p-cresol that was a glutathione depletory, and

the furan ring of the diterpenoids in germander was oxidized by CYP3A4 to reactive epoxide which reacts with proteins such as CYP3A and epoxide hydrolase. On the other hand, some herbal/dietary constituents were shown to form reactive intermediates capable of irreversibly inhibiting various CYPs. The resultant metabolites lead to CYP inactivation by chemical modification of the heme, the apoprotein, or both as a result of covalent binding of modified heme to the apoprotein. Some examples include bergamottin, a furanocoumarin of grapefruit juice; capsaicin from chili peppers; glabridin, an isoflavan from licorice root; isothiocyanates found in all cruciferous vegetables; oleuropein rich in olive oil; diallyl sulfone found in garlic; and resveratrol, a constituent of red wine. CYPs have been known to metabolize more than 95% therapeutic drugs and activate a number of procarcinogens as well. Therefore, mechanism-based inhibition of CYPs may provide an explanation for some reported herb-drug interactions and chemopreventive activity of herbs. Due to the wide use and easy availability of herbal medicines, there is increasing concern about herbal toxicity. The safety and quality of herbal medicine should be ensured through greater research, pharmacovigilance, greater regulatory control and better communication between patients and health professionals.

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ACCESSION NUMBER: 2004355686 EMBASE  
 TITLE: Olives and olive oil in **cancer** prevention.  
 AUTHOR: Owen R.W.; Haubner R.; Wurtele G.; Hull W.E.; Spiegelhalder B.; Bartsch H.  
 CORPORATE SOURCE: R.W. Owen, Div. Toxicol. Cancer Risk Factors, German Cancer Research Center, Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany. R.Owen@DKFZ-Heidelberg.de  
 SOURCE: European Journal of Cancer Prevention, (2004) Vol. 13, No. 4, pp. 319-326. .  
 Refs: 28  
 ISSN: 0959-8278 CODEN: EJUPEK  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20040909  
 Last Updated on STN: 20040909  
 AB Epidemiologic studies conducted in the latter part of the twentieth century demonstrate fairly conclusively that the people of the Mediterranean basin enjoy a healthy lifestyle with decreased incidence of degenerative diseases. The data show that populations within Europe that consume the so-called 'Mediterranean diet' have lower incidences of major illnesses such as **cancer** and cardiovascular disease. Studies have suggested that the health-conferring benefits of the Mediterranean diet are due mainly to a high consumption of fibre, fish, fruits and vegetables. More recent research has focused on other important factors such as olives and olive oil. Obviously fibre (especially wholegrain-derived products), fruits and vegetables supply an important source of dietary antioxidants. What is the contribution from olives and olive oil? Apparently the potential is extremely high but epidemiologic studies rarely investigate consumption of these very important products



in-depth, perhaps due to a lack of exact information on the types and amounts of antioxidants present. Recent studies have shown that olives and olive oil contain antioxidants in abundance. Olives (especially those that have not been subjected to the Spanish brining process) contain up to 16 g/kg typified by acteosides, hydroxytyrosol, tyrosol and phenyl propionic acids. Olive oil, especially extra virgin, contains smaller amounts of hydroxytyrosol and tyrosol, but also contains secoiridoids and lignans in abundance. Both olives and olive oil contain substantial amounts of other compounds deemed to be **anticancer** agents (e.g. squalene and terpenoids) as well as the peroxidation-resistant lipid oleic acid. It seems probable that olive and olive oil consumption in southern Europe represents an important contribution to the beneficial effects on health of the Mediterranean diet. .COPYRG. 2004 Lippincott Williams & Wilkins.

L14 ANSWER 11 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
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ACCESSION NUMBER: 2004:350361 BIOSIS  
DOCUMENT NUMBER: PREV200400348082  
TITLE: Production of highly purified hydroxytyrosol from Olea europaea leaf extract biotransformed by hyperthermophilic beta-glycosidase.  
AUTHOR(S): Briante, Raffaella; Patumi, Maurizio; Febbraio, Ferdinando; Nucci, Roberto [Reprint Author]  
CORPORATE SOURCE: Ist Biochim Prot, CNR, Via Marconi 10, I-80125, Naples, Italy  
r.nucci@ibp.cnr.it  
SOURCE: Journal of Biotechnology, (July 1 2004) Vol. 111, No. 1, pp. 67-77. print.  
ISSN: 0168-1656 (ISSN print).  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 18 Aug 2004  
Last Updated on STN: 18 Aug 2004

AB A large amount of highly purified hydroxytyrosol (91-94% in weight) is obtained in short time by a simple biotransformation of Olea europaea leaf extract by a partially purified hyperthermophilic beta-glycosidase immobilized on chitosan support. The biotransformation conditions have been modulated for increasing the hydroxytyrosol yield, whilst chitosan and chitin matrices are used as adsorbent materials in liquid phase hydroxytyrosol extraction from the biotransformed mixtures. Natural and non-toxic hydroxytyrosol has been by this way produced from a vegetal source, and this compound appeared for the first time highly purified by natural and biocompatible safe biopolymers in comparison to previous results. Moreover, the GC analyses have displayed that the eluates from a two-step bioreactor have qualitative composition very similar to that of the extra-virgin olive oil polar fraction. The proposed bioreactor could also find application in the utilization of olive mill waste waters (OMWW), medium rich in large amounts of oleuropein, which can be converted in pharmacologically active compounds. Copyright 2004 Elsevier B.V. All rights reserved.

L14 ANSWER 12 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN

ACCESSION NUMBER: 2005:122403 BIOSIS  
DOCUMENT NUMBER: PREV200500125839  
TITLE: Olive oil and oxidative stress.  
AUTHOR(S): Visioli, Francesco [Reprint Author]; Bogani, Paola;

10/712423

CORPORATE SOURCE: Grande, Simona; Gail, Claudio  
Dept Pharmacol Sci, Univ Milan, Milan, Italy  
francesco.visioli@unini.it  
SOURCE: Grasas y Aceites, (January 2004) Vol. 55, No. 1, pp.  
66-75. print.  
ISSN: 0017-3495 (ISSN print).  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 1 Apr 2005  
Last Updated on STN: 1 Apr 2005

AB In addition to the fatty acid profile of olive oil, which is high in the monounsaturated oleic acid and appears to be beneficial in reducing several risk factors for coronary heart disease and certain **cancers**, extra virgin olive oil contains a considerable amount of phenolic compounds, e.g. hydroxytyrosol and oleuropein, that are responsible for its peculiar taste and for its high stability. A body of evidence demonstrates that olive oil phenolics are powerful antioxidants. Although most of these studies have been carried out in vitro, some in vivo experiments confirm that olive oil phenolics are dose-dependently absorbed and that they retain their biological activities after ingestion. These data could in part explain the lower incidence of coronary heart disease in the Mediterranean area, where (extra virgin) olive oil is the principal source of fat.

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on STN

ACCESSION NUMBER: 2004:378026 BIOSIS  
DOCUMENT NUMBER: PREV200400378017  
TITLE: Differential anti-inflammatory effects of phenolic compounds from olive oil identified in human whole blood cultures.  
AUTHOR(S): Miles, E. A. [Reprint Author]; Zoubouli, R.; Calder, P. C.  
CORPORATE SOURCE: Sch MedInst Human Nutr, Univ Southampton, Southampton, Hants, SO16 7PX, England  
SOURCE: Chemistry and Physics of Lipids, (June 2004) Vol. 130, No. 1, pp. 34-35. print.  
Meeting Info.: 45th International Conference on the Bioscience of Lipids. Ioannina, Greece. May 25-29, 2004.  
ISSN: 0009-3084 (ISSN print).  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 22 Sep 2004  
Last Updated on STN: 22 Sep 2004

L14 ANSWER 14 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN DUPLICATE 4

ACCESSION NUMBER: 2004:368865 BIOSIS  
DOCUMENT NUMBER: PREV200400370276  
TITLE: Involvement of oleuropein in (some) digestive metabolic pathways.  
AUTHOR(S): Polzonetti, V.; Egidi, D.; Vita, A.; Vincenzetti, S.; Natalini, P. [Reprint Author]  
CORPORATE SOURCE: Dipartimento Sci Morfologiche and Biochim Comparete, Univ Camerino, Via Camerini 2, I-62032, Camerino, Italy  
paolo.natalini@unicam.it  
SOURCE: Food Chemistry, (November 2004) Vol. 88, No. 1, pp.

Searcher : Shears 571-272-2528

10/712423

11-15. print.

CODEN: FOCHDJ. ISSN: 0308-8146.

DOCUMENT TYPE:

Article

LANGUAGE:

English

ENTRY DATE:

Entered STN: 8 Sep 2004

Last Updated on STN: 8 Sep 2004

AB Olive oil is the principal source of fats in the Mediterranean diet and it has been postulated that the components in olive oil can contribute to a lower incidence of coronary heart disease and **cancers** (prostate, colon, breast, and skin). The positive effects on human health can be attributed to the high level of phenolic compounds present in olive oil, the major ones being oleuropein, hydroxytyrosol and tyrosol. The aim of the present study was to evaluate the effect of oleuropein on enzymes involved in specific pathways of metabolism of proteins, carbohydrates and lipids. In particular, the effects of oleuropein on enzymes, such as trypsin, pepsin, lipase, glycerol dehydrogenase, glycerol-3-phosphate dehydrogenase, and glycerokinase, were investigated. Results demonstrate that oleuropein is able to activate pepsin and shows an inhibitory effect toward all the other enzymes tested, which suggests a new role for this polyphenol. In addition, a new method for lipase activity assay is presented. Copyright 2004 Elsevier Ltd, All rights reserved.

L14 ANSWER 15 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN DUPLICATE 5

ACCESSION NUMBER: 2003:497686 BIOSIS

DOCUMENT NUMBER: PREV200300499640

TITLE: In vitro cytotoxicity to human cells in culture of some phenolics from olive oil.

AUTHOR(S): Babich, H. [Reprint Author]; Visioli, F.

CORPORATE SOURCE: Department of Biology, Stern College for Women, Yeshiva University, 245 Lexington Avenue, New York, NY, 10016, USA  
babich@ymail.yu.edu

SOURCE: Farmaco (Lausanne), (May 2003) Vol. 58, No. 5, pp. 403-407. print.  
ISSN: 0014-827X.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Oct 2003

Last Updated on STN: 29 Oct 2003

AB The neutral red in vitro cytotoxicity assay was used to evaluate the comparative responses of human cells isolated from tissues of the oral cavity to olive oil phenolics. The cell lines used included normal gingival fibroblasts, immortalized, nontumorigenic gingival epithelial cells, and **carcinoma** cells from the salivary gland. No differences in the relative sensitivities to the phenolics amongst the three cell types were noted. In general, for all cell types, the sequence of increasing cytotoxicity was: oleuropein aglycone>oleuropein glycoside, caffeic acid>o-coumaric acid>cinnamic acid>hydroxytyrosol, syringic acid, protocatechuic acid, vanillic acid. Cytotoxicity was noted only at phenolic concentrations far exceeding those attainable after habitual consumption, thus indicating that consumption of phenol-rich olive oil is safe.

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ACCESSION NUMBER: 2004280692 EMBASE

Searcher : Shears 571-272-2528

10/712423

TITLE: Natural products and synthetic compounds as immunomodulators.  
AUTHOR: Kayser O.; Masihi K.N.; Kiderlen A.F.  
CORPORATE SOURCE: Dr. A.F. Kiderlen, Robert Koch-Institut, Department of Infectious Diseases, Cellular Defense Mechanisms Unit, Nordufer 20, D-13353 Berlin, Germany  
SOURCE: Expert Review of Anti-Infective Therapy, (2003) Vol. 1, No. 2, pp. 319-335. .  
Refs: 191  
ISSN: 1478-7210 CODEN: ERATCK  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20040722  
Last Updated on STN: 20040722

AB Research on immunomodulation by natural products or synthetic derivatives is of key interest for anti-infective therapy for a number of reasons. Many plant remedies well-known in traditional medicine or refined natural products in clinical use exert their anti-infective effects not only (if at all) by directly affecting the pathogen. At least part of their effect is indirect, by stimulating natural and adaptive defense mechanisms of the host. These findings have now given many empirical therapies a rationale, scientific basis and thereby a means for 'intelligent' improvement. In discovering the molecular mechanisms by which known remedies exert their effects, chosen elements further down the 'chain of command' might be synthesized and applied directly for more rapid and selective cure, omitting unwanted side effects. The direct use of recombinant cytokines, often in combination with antibiotics, is one consequence of this rationale. .COPYRGHT. Future Drugs Ltd. All rights reserved.

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ACCESSION NUMBER: 2003069313 EMBASE  
TITLE: Olive-oil consumption and cancer risk.  
AUTHOR: Filik L.; Ozyilkan O.  
SOURCE: European Journal of Clinical Nutrition, (1 Jan 2003) Vol. 57, No. 1, pp. 191. .  
Refs: 4  
ISSN: 0954-3007 CODEN: EJCNEQ  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Letter  
FILE SEGMENT: 016 Cancer  
017 Public Health, Social Medicine and Epidemiology  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20030220  
Last Updated on STN: 20030220

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L14 ANSWER 18 OF 35 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2003067119 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12535851  
TITLE: Simultaneous determination of oleuropein and hydroxytyrosol in rat plasma using liquid

Searcher : Shears 571-272-2528

10/712423

chromatography with fluorescence detection.  
AUTHOR: Tan Hai-Wei; Tuck Kellie L; Stupans Ieva; Hayball Peter J  
CORPORATE SOURCE: Centre for Pharmaceutical Research, School of  
Pharmaceutical, Molecular and Biomedical Sciences,  
University of South Australia, Adelaide, 5000,  
Australia.  
SOURCE: Journal of chromatography. B, Analytical technologies  
in the biomedical and life sciences, (2003 Feb 25) Vol.  
785, No. 1, pp. 187-91.  
Journal code: 101139554. ISSN: 1570-0232.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200307  
ENTRY DATE: Entered STN: 20030212  
Last Updated on STN: 20030801  
Entered Medline: 20030731

AB Oleuropein, the main glycoside present in olives, and hydroxytyrosol, the principal degradation product of oleuropein present in olive oil, have been linked to reduction of coronary heart disease and certain **cancers**. In the present study a direct and sensitive reversed-phase high-performance liquid chromatographic assay was developed for simultaneous quantification of both oleuropein and hydroxytyrosol. The plasma protein was precipitated with acetonitrile, samples were then centrifuged and supernatants were dried, and reconstituted with water prior to injection. The chromatographic analysis was carried out using a phenyl column and an isocratic elution of acidified water and acetonitrile with fluorescence detection at 281 and 316 nm for excitation and emission, respectively. The calibration curve was linear and limits of quantification were 30 ng/ml and 3 microg/ml for hydroxytyrosol and oleuropein, respectively. The method has been successfully applied to monitor oleuropein and hydroxytyrosol plasma levels in the rat.

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ACCESSION NUMBER: 2003243873 EMBASE  
TITLE: UV-induced skin damage.  
AUTHOR: Ichihashi M.; Ueda M.; Budiyo A.; Bito T.; Oka M.;  
Fukunaga M.; Tsuru K.; Horikawa T.  
CORPORATE SOURCE: M. Ichihashi, Division of Dermatology, Dept. of  
Clinical Molecular Medicine, Kobe Univ. Grad. School of  
Medicine, 7-5-1, Kusunoki-cho, Chuo-ku, Kobe 650-0017,  
Japan. ichihashi@med.kobe.ac.jp  
SOURCE: Toxicology, (15 Jul 2003) Vol. 189, No. 1-2, pp. 21-39.  
Refs: 135  
ISSN: 0300-483X CODEN: TXCYAC  
COUNTRY: Ireland  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 013 Dermatology and Venereology  
016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
052 Toxicology  
LANGUAGE: English  
SUMMARY LANGUAGE: English

Searcher : Shears 571-272-2528

10/712423

ENTRY DATE: Entered STN: 20030703  
Last Updated on STN: 20030703

AB Solar radiation induces acute and chronic reactions in human and animal skin. Chronic repeated exposures are the primary cause of benign and malignant skin **tumors**, including malignant melanoma. Among types of solar radiation, ultraviolet B (290-320 nm) radiation is highly mutagenic and **carcinogenic** in animal experiments compared to ultraviolet A (320-400 nm) radiation. Epidemiological studies suggest that solar UV radiation is responsible for skin **tumor** development via gene mutations and immunosuppression, and possibly for photoaging. In this review, recent understanding of DNA damage caused by direct UV radiation and by indirect stress via reactive oxygen species (ROS) and DNA repair mechanisms, particularly nucleotide excision repair of human cells, are discussed. In addition, mutations induced by solar UV radiation in p53, ras and patched genes of non-melanoma skin **cancer** cells, and the role of ROS as both a promoter in UV-**carcinogenesis** and an inducer of UV-apoptosis, are described based primarily on the findings reported during the last decade. Furthermore, the effect of UV on immunological reaction in the skin is discussed. Finally, possible prevention of UV-induced skin **cancer** by feeding or topical use of antioxidants, such as polyphenols, vitamin C, and vitamin E, is discussed. .COPYRG. 2003 Published by Elsevier Science Ireland Ltd.

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ACCESSION NUMBER: 2003035183 EMBASE  
TITLE: The randomized controlled trial in studies using biomarkers.  
AUTHOR: Vineis P.  
CORPORATE SOURCE: P. Vineis, Dipt. di Sci. Biomed. e Oncol. Umana, University of Torino, via Santena 7, Torino, Italy. paolo.vineis@unito.it  
SOURCE: Biomarkers, (2003) Vol. 8, No. 1, pp. 13-32. .  
Refs: 21  
ISSN: 1354-750X CODEN: BIOMFA  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 016 Cancer  
017 Public Health, Social Medicine and Epidemiology  
028 Urology and Nephrology  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20030130  
Last Updated on STN: 20030130

AB The randomized controlled trial (RCT) is a scientific experiment during which observations on the effects of therapy or a preventive action are conducted by the researcher under rigorous control. The purpose of the experiment is to clear the uncertainties surrounding a clinical/research issue and involves isolating the 'treatment' and 'end result' variables from external influences. RCTs therefore make use of scientific method standards: measuring, which includes the possibility of reproducing observations; controlling factors unconnected to the cause-effect relationship of interest; and the external verification or 'falsification' of the cause-effect

Searcher : Shears 571-272-2528

relationship. Many RCTs are now including biomarkers to answer scientific questions in a more accurate way. In the present methodological paper, the main aspects involved in the design and conduction of a trial are discussed, with special emphasis on the use of biomarkers. Aspects that are often overlooked by scientists involved in the design of trials include multiple comparisons, subgroup analysis, the duration of the observations, the use of surrogate endpoints, and ethical issues. This review summarizes the main issues that should be addressed in a protocol, and illustrates these with an example.

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ACCESSION NUMBER: 2002286207 EMBASE  
 TITLE: Exocyclic DNA adducts as oxidative stress markers in colon **carcinogenesis**: Potential role of lipid peroxidation, dietary fat and antioxidants.  
 AUTHOR: Bartsch H.; Nair J.; Owen R.W.  
 CORPORATE SOURCE: H. Bartsch, Div. of Toxicol./Cancer Risk Factors, German Cancer Research Center DKFZ, Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany  
 SOURCE: Biological Chemistry, (2002) Vol. 383, No. 6, pp. 915-921. .  
 Refs: 47  
 ISSN: 1431-6730 CODEN: BICHF3  
 COUNTRY: Germany  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 048 Gastroenterology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20020829  
 Last Updated on STN: 20020829

AB Molecular pathways to colorectal **cancer** involve multiple genetic changes, whereby extensive oxyradical damage causes mutations in **cancer**-related genes and leads to a cycle of cell death and regeneration. Besides direct oxidative DNA-damage, reactive oxygen and nitrogen species can induce etheno ( $\epsilon$ )-DNA adducts mainly via trans-4-hydroxy-2-nonenal, generated as the major aldehyde by lipid peroxidation (LPO) of  $\omega$ -6 PUFAs. Patients with familial adenomatous polyposis (FAP) develop multiple colorectal adenomas. In affected tissues increased LPO could be triggered due to increased arachidonic acid metabolism as a result of elevated cyclooxygenase. Our studies demonstrated an increased  $\epsilon$ -DNA adduct level in affected colon epithelia of FAP patients.  $\epsilon$ -DNA adducts are promutagenic and can cause genomic instability that drives colorectal adenoma to malignancy. We have further investigated the potential chemopreventive properties of olive oil and its polyphenolic components. 'Mediterranean diet', of which olive oil is a major fatty acid source, has protective effects against human breast and colorectal **cancers**. Olive oil extracts and the newly identified lignan fractions showed high antioxidant capacity in vitro. As  $\epsilon$ -DNA adducts are biomarkers for oxidative stress and LPO induced DNA damage, they can verify the efficacy of newly identified antioxidants, e.g. from olive oil, as chemopreventive agents against colon **carcinogenesis**.

L14 ANSWER 22 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN DUPLICATE 7

ACCESSION NUMBER: 2003:57519 BIOSIS  
DOCUMENT NUMBER: PREV200300057519  
TITLE: Major phenolic compounds in olive oil: Metabolism and health effects.  
AUTHOR(S): Tuck, Kellie L. [Reprint Author]; Hayball, Peter J.  
CORPORATE SOURCE: Centre for Pharmaceutical Research, School of Pharmaceutical, Molecular and Biomedical Sciences, University of South Australia, Adelaide, 5000, Australia  
kellie.tuck@unisa.edu.au  
SOURCE: Journal of Nutritional Biochemistry, (November 2002) Vol. 13, No. 11, pp. 636-644. print.  
CODEN: JNBIEL. ISSN: 0955-2863.  
DOCUMENT TYPE: Article  
General Review; (Literature Review)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 22 Jan 2003  
Last Updated on STN: 22 Jan 2003

AB It has been postulated that the components in olive oil in the Mediterranean diet, a diet which is largely vegetarian in nature, can contribute to the lower incidence of coronary heart disease and prostate and colon cancers. The Mediterranean diet includes the consumption of large amounts of olive oil. Olive oil is a source of at least 30 phenolic compounds. The major phenolic compounds in olive oil are oleuropein, hydroxytyrosol and tyrosol. Recently there has been a surge in the number of publications that has investigated their biological properties. The phenolic compounds present in olive oil are strong antioxidants and radical scavengers. Olive "waste water" also possesses compounds which are strong antioxidant and radical scavengers. Typically, hydroxytyrosol is a superior antioxidant and radical scavenger to oleuropein and tyrosol. Hydroxytyrosol and oleuropein have antimicrobial activity against ATTC bacterial strains and clinical bacterial strains. Recent syntheses of labeled and unlabelled hydroxytyrosol coupled with superior analytical techniques have enabled its absorption and metabolism to be studied. It has recently been found that hydroxytyrosol is renally excreted unchanged and as the following metabolites as its glucuronide conjugate, sulfate conjugate, homovanillic acid, homovanillic alcohol, 3,4-dihydroxyphenylacetic acid and 3,4-dihydroxyphenylacetaldehyde. Studies with tyrosol have shown that it is excreted unchanged and as its conjugates. This review summarizes the antioxidant abilities; the scavenging abilities and the biological fates of hydroxytyrosol, oleuropein and tyrosol which have been published in recent years.

L14 ANSWER 23 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN DUPLICATE 8

ACCESSION NUMBER: 2002:535154 BIOSIS  
DOCUMENT NUMBER: PREV200200535154  
TITLE: Olive oil phenolics: Effects on DNA-oxidation and redox enzyme mRNA in prostate cells.  
AUTHOR(S): Lund, Elizabeth [Reprint author]  
CORPORATE SOURCE: Institute of Food Research, Norwich Research Park, Colney, Norwich, NR4 7UA, UK  
SOURCE: British Journal of Nutrition, (September, 2002) Vol. 88, No. 3, pp. 223-224. print.  
CODEN: BJNUAV. ISSN: 0007-1145.



10/712423

DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 16 Oct 2002  
Last Updated on STN: 5 Dec 2002

L14 ANSWER 24 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN

ACCESSION NUMBER: 2002:421390 BIOSIS  
DOCUMENT NUMBER: PREV200200421390  
TITLE: Biological properties of olive oil phytochemicals.  
AUTHOR(S): Visioli, Francesco [Reprint author]; Galli, Claudio  
CORPORATE SOURCE: University of Milan, Institute of Pharmacological  
Sciences, Via Balzaretti 9, 20133, Milan, Italy  
francesco.visioli@unimi.it  
SOURCE: Critical Reviews in Food Science and Nutrition, (May,  
2002) Vol. 42, No. 3, pp. 209-221. print.  
ISSN: 1040-8398.  
DOCUMENT TYPE: Article  
General Review; (Literature Review)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 7 Aug 2002  
Last Updated on STN: 7 Aug 2002

L14 ANSWER 25 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN

ACCESSION NUMBER: 2002:143530 BIOSIS  
DOCUMENT NUMBER: PREV200200143530  
TITLE: Antioxidant and other biological activities of phenols  
from olives and olive oil.  
AUTHOR(S): Visioli, Francesco [Reprint author]; Poli, Andrea;  
Galli, Claudio  
CORPORATE SOURCE: Department of Pharmacological Sciences, University of  
Milan, Via Balzaretti 9, 20133, Milan, Italy  
francesco.visioli@unimi.it  
SOURCE: Medicinal Research Reviews, (January, 2002) Vol. 22,  
No. 1, pp. 65-75. print.  
CODEN: MRREDD. ISSN: 0198-6325.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 14 Feb 2002  
Last Updated on STN: 26 Feb 2002

L14 ANSWER 26 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
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ACCESSION NUMBER: 2001:417654 BIOSIS  
DOCUMENT NUMBER: PREV200100417654  
TITLE: Water-soluble extract from olives.  
AUTHOR(S): Crea, Roberto [Inventor]; Caglioti, Luciano [Inventor,  
Reprint author]  
CORPORATE SOURCE: Rome, Italy  
ASSIGNEE: CreAgri L.L.C., Hayward, CA, USA  
PATENT INFORMATION: US 6197308 20010306  
SOURCE: Official Gazette of the United States Patent and  
Trademark Office Patents, (Mar. 6, 2001) Vol. 1244, No.  
1. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 29 Aug 2001

Searcher : Shears 571-272-2528

Last Updated on STN: 22 Feb 2002

AB The invention provides olive-derived vegetation water substantially free of monophenolic compounds (e.g., tyrosol and its derivatives) from olive pits. According to one aspect of the invention, the pits or seeds are removed from the olives prior to pressing. The pitless pulp or meat is then pressed to obtain a liquid-phase mixture including olive oil, vegetation water, and solid by-products. The vegetation water is separated from the rest of the liquid-phase mixture and collected. The vegetation water is useful as a source of oleuropein.

L14 ANSWER 27 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
on STN DUPLICATE 9

ACCESSION NUMBER: 2001:522398 BIOSIS  
DOCUMENT NUMBER: PREV200100522398  
TITLE: The inhibitory effects of compounds from olive leaf on **tumor** necrosis factor production and on beta-hexosaminidase release.  
AUTHOR(S): Nishibe, Sansei [Reprint author]; Han, Yingmei [Reprint author]; Noguchi, Yukari [Reprint author]; Ueda, Hiroshi; Yamazaki, Masatoshi; Mizutani, Kenji; Kambara, Toshimitsu; Kishida, Naoko  
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido, 061-0293, Japan  
SOURCE: Natural Medicines, (August, 2001) Vol. 55, No. 4, pp. 205-208. print.  
ISSN: 1340-3443.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 7 Nov 2001  
Last Updated on STN: 23 Feb 2002

AB The extraction and isolation of olive leaf gave luteolin 7-O-glucoside, luteolin 4'-O-glucoside and oleuropein as the major components. The inhibitory effects of these compounds on **tumor** necrosis factor (TNF-alpha) production and on beta-hexosaminidase release from rat basophilic leukemia (RBL-2H3) cells, which were both recently found to be linked to allergic reaction, were examined. Oleuropein showed a potent inhibitory effect on TNF-alpha production. Luteolin 4'-O-glucoside showed a strong inhibitory effect on beta-hexosaminidase release (IC50: 17.1 mug/ml).

L14 ANSWER 28 OF 35 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 2001098429 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11110859  
TITLE: Oleuropein, an antioxidant polyphenol from olive oil, is poorly absorbed from isolated perfused rat intestine.  
AUTHOR: Edgecombe S C; Stretch G L; Hayball P J  
CORPORATE SOURCE: Centre for Pharmaceutical Research, University of South Australia, North Terrace, Adelaide, South Australia, 5000, Australia.  
SOURCE: The Journal of nutrition, (2000 Dec) Vol. 130, No. 12, pp. 2996-3002.  
Journal code: 0404243. ISSN: 0022-3166.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals

Searcher : Shears 571-272-2528

10/712423

ENTRY MONTH: 200102  
ENTRY DATE: Entered STN: 20010322  
Last Updated on STN: 20010322  
Entered Medline: 20010201

AB Epidemiological studies have shown that the incidence of heart disease and certain **cancers** is lower in the Mediterranean region. This has been attributed to the high consumption of olive oil in the Mediterranean diet, which contains polyphenolic compounds with antioxidant activity. Although many in vitro studies have been performed to elucidate mechanisms by which these compounds may act, there are virtually no data relating to their fate after ingestion. Therefore, we decided to investigate the intestinal absorption of one of the major olive oil polyphenolics, oleuropein. To do this, a novel in situ intestinal perfusion technique was developed, and the absorption of oleuropein was studied under both iso-osmotic and hypotonic luminal conditions. Oleuropein was absorbed, with an apparent permeability coefficient ( $P_{app}$ ) of  $1.47 \pm 0.13 \times 10^{-6}$  cm/s ( $\pm$  SE) observed under iso-osmotic conditions. The mechanism of absorption is unclear but may involve transcellular transport (SGLT1) or paracellular movement. Under hypotonic conditions, the permeability of oleuropein was significantly greater ( $5.92 \pm 0.49 \times 10^{-6}$  cm/s,  $P < 0.001$ ). This increase is thought to be due to an increase in paracellular movement facilitated by the opening of paracellular junctions in response to hypotonicity. Overall, we determined that the olive oil polyphenolic oleuropein can be absorbed, albeit poorly, from isolated perfused rat intestine. Therefore, it is possible that it or its metabolites may confer a positive health benefit after the consumption of olive oil, most likely via an antioxidant mechanism.

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ACCESSION NUMBER: 2000409319 EMBASE  
TITLE: Protective effect of topically applied olive oil against photocarcinogenesis following UVB exposure of mice.  
AUTHOR: Budiyanto A.; Ahmed N.U.; Wu A.; Bito T.; Nikaido O.; Osawa T.; Ueda M.; Ichihashi M.  
CORPORATE SOURCE: M. Ueda, Department of Dermatology, Kobe University School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan. [mueda@med.kobe-u.ac.jp](mailto:mueda@med.kobe-u.ac.jp)  
SOURCE: Carcinogenesis, (2000) Vol. 21, No. 11, pp. 2085-2090.

Refs: 31  
ISSN: 0143-3334 CODEN: CRNGDP  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 013 Dermatology and Venereology  
016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
052 Toxicology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20001213  
Last Updated on STN: 20001213

AB Reactive oxygen species have been shown to play a role in ultraviolet light (UV)-induced skin **carcinogenesis**. Vitamin E and green tea polyphenols reduce experimental skin **cancers** in mice

Searcher : Shears 571-272-2528

mainly because of their antioxidant properties. Since olive oil has also been reported to be a potent antioxidant, we examined its effect on UVB-induced skin **carcinogenesis** in hairless mice. Extra-virgin olive oil was applied topically before or after repeated exposure of mice to UVB. The onset of UVB-induced skin **tumors** was delayed in mice painted with olive oil compared with UVB control mice. However, with increasing numbers of UVB exposures, differences in the mean number of **tumors** between UVB control mice and mice pretreated with olive oil before UVB exposure (pre-UVB group) were lost. In contrast, mice that received olive oil after UVB exposure (post-UVB group) showed significantly lower numbers of **tumors** per mouse than those in the UVB control group throughout the experimental period. The mean number of **tumors** per mouse in the UVB control, pre-UVB and post-UVB groups was 7.33, 6.69 and 2.64, respectively, in the first experiment, and 8.53, 9.53 and 3.36 in the second experiment. Camellia oil was also applied, using the same experimental protocol, but did not have a suppressive effect. Immunohistochemical analysis of DNA damage in the form of cyclobutane pyrimidine dimers (CPD), (6-4) photoproducts and 8-hydroxy-2'-deoxyguanosine (8-OHdG) in samples taken 30 min after a single exposure of UVB showed no significant difference between UVB-irradiated control mice and the pre-UVB group. In the post-UVB group, there were lower levels of 8-OHdG in epidermal nuclei, but the formation of CPD and (6-4) photoproducts did not differ. Exposure of olive oil to UVB before application abrogated the protective effect on 8-OHdG formation. These results indicate that olive oil topically applied after UVB exposure can effectively reduce UVB-induced murine skin **tumors**, possibly via its anti-oxidant effects in reducing DNA damage by reactive oxygen species, and that the effective component may be labile to UVB.

L14 ANSWER 30 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
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ACCESSION NUMBER: 2000:236012 BIOSIS  
DOCUMENT NUMBER: PREV200000236012  
TITLE: Skin anti-inflammatory activity of hydroxytyrosol and its acid form 3,4 dihydroxyphenylacetic acid.  
AUTHOR(S): Despotopoulos, A. [Reprint author]; Rallis, M. [Reprint author]; Marakos, P. [Reprint author]; Rodis, P.; Proxenia, N.; Demetzos, C. [Reprint author]; Xenos, K.; Katsarou, A.; Tsaldaris, I. [Reprint author]; Papaioannou, G. [Reprint author]  
CORPORATE SOURCE: University of Athens, Athens, Greece  
SOURCE: Journal of Investigative Dermatology, (April, 2000) Vol. 114, No. 4, pp. 881. print.  
Meeting Info.: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA. May 10-14, 2000.  
CODEN: JIDEAE. ISSN: 0022-202X.  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 7 Jun 2000  
Last Updated on STN: 5 Jan 2002

L14 ANSWER 31 OF 35 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2000163671 EMBASE  
TITLE: [Polyphenols: Simple structures with high potency].

10/712423

POLYPHENOLE: EINFACHE STRUKTUREN MIT HOHEM POTENZIAL.  
AUTHOR: Metz G.  
CORPORATE SOURCE: Dr. G. Metz, Auf dem Rucken 29, 89146 Blaubeuren,  
Germany  
SOURCE: Pharmazeutische Zeitung, (20 Apr 2000) Vol. 145, No.  
16, pp. 23-28. .  
Refs: 6  
ISSN: 0031-7136 CODEN: PZSED5  
COUNTRY: Germany  
DOCUMENT TYPE: Journal; (Short Survey)  
FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: German  
ENTRY DATE: Entered STN: 20000525  
Last Updated on STN: 20000525  
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L14 ANSWER 32 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
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ACCESSION NUMBER: 2000:397299 BIOSIS  
DOCUMENT NUMBER: PREV200000397299  
TITLE: Studies on constituents with cytotoxic activity from  
the stem bark of Syringa velutina.  
AUTHOR(S): Park, Hee-Juhn; Lee, Myung-Sun; Lee, Kyung-Tae; Sohn,  
Il-Cheol; Han, Yong-Nam; Miyamoto, Ken-ichi [Reprint  
author]  
CORPORATE SOURCE: Department of Pharmacology and Pharmaceutics, Graduate  
School of Natural Science and Technology, Kanazawa  
University, 13-1 Takara-machi, Kanazawa, 920-9042,  
Japan  
SOURCE: Chemical and Pharmaceutical Bulletin (Tokyo), (July,  
1999) Vol. 47, No. 7, pp. 1029-1031. print.  
CODEN: CPBTAL. ISSN: 0009-2363.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20 Sep 2000  
Last Updated on STN: 8 Jan 2002

AB Cytotoxic compounds, oleuropein (1) and a phenylethanoid glycoside (2)  
were isolated from the stem bark of Syringa velutina KOM. along with  
coniferylaldehyde 4-O-glucoside, syringin, ligstroside,  
(+)-syringaresinol 4-O-glucoside, (+)-medioresinol 4'-O-glucoside and  
(-)-olivil 4'-O-glucoside. Phenylethanoid glycoside (2) was  
identified to be 3,4-dihydroxyphenylethyl alcohol 8-O-beta-D-  
glucopyranoside. This compound showed the most potent cytotoxic  
effect on several tumor cell lines (P-388, L-1210, SNU-5 and  
HL-60) among eight compounds isolated in the present study. We  
suggest that the 3,4-dihydroxyphenylethoxy moiety of this compound  
contributes to cytotoxicity.

L14 ANSWER 33 OF 35 MEDLINE on STN DUPLICATE 11  
ACCESSION NUMBER: 1998124113 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9464466  
TITLE: Oleuropein, the bitter principle of olives, enhances  
nitric oxide production by mouse macrophages.  
AUTHOR: Visioli F; Bellosta S; Galli C  
CORPORATE SOURCE: Institute of Pharmacological Sciences, Milan, Italy..  
Francesco.Visioli@unimi.it  
SOURCE: Life sciences, (1998) Vol. 62, No. 6, pp. 541-6.  
Journal code: 0375521. ISSN: 0024-3205.

Searcher : Shears 571-272-2528

10/712423

PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199802  
ENTRY DATE: Entered STN: 19980226  
Last Updated on STN: 19980226  
Entered Medline: 19980219

AB The Mediterranean diet, rich in fresh fruits and vegetables, has been associated with a lower incidence of cardiovascular disease and **cancer**, partly because of its high proportion of bioactive compounds such as vitamins, flavonoids and polyphenols. The major lipid component of such diet is the drupe-derived olive oil, that can be distinguished from other seed oils for the peculiar composition of its non-triglyceride fraction. In fact, several minor components, including polyphenols, grant the oil its particular taste and aroma. Oleuropein, the most abundant among these components, has been shown to be a potent antioxidant endowed with antiinflammatory properties. We investigated the effects of oleuropein on NO release in cell culture and its activity toward nitric oxide synthase (iNOS) expression. The results show that oleuropein dose-dependently enhance nitrite production in LPS-challenged mouse macrophages. This effect was blocked by the iNOS inhibitor L-NAME, indicating increased iNOS activity. Also, Western blot analysis of cell homogenates show that oleuropein increases iNOS expression in such cells. Taken together, our data suggest that, during endotoxin challenge, oleuropein potentiates the macrophage-mediated response, resulting in higher NO production, currently believed to be beneficial for cellular and organismal protection.

L14 ANSWER 34 OF 35 MEDLINE on STN  
ACCESSION NUMBER: 1998456830 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9786644  
TITLE: Cytostatic activity of some compounds from the unsaponifiable fraction obtained from virgin olive oil.  
AUTHOR: Saenz M T; Garcia M D; Ahumada M C; Ruiz V  
CORPORATE SOURCE: Laboratori do Farmacognosia, Universidad de Sevilla, 41012 Seville, Spain.  
SOURCE: Farmaco (Societa chimica italiana : 1989), (1998 Jun 30) Vol. 53, No. 6, pp. 448-9.  
Journal code: 8912641. ISSN: 0014-827X.  
PUB. COUNTRY: Italy  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199810  
ENTRY DATE: Entered STN: 19981029  
Last Updated on STN: 19981029  
Entered Medline: 19981022

AB Oleuropein, tyrosol, squalene and the fraction of sterols and triterpenoid dialcohols from the unsaponifiable fraction obtained from virgin olive oil have been tested for possible cytostatic activity against McCoy cells, using 6-mercaptopurine as a positive control. The samples of sterols and triterpenic dialcohols showed a strong activity.

L14 ANSWER 35 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation  
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ACCESSION NUMBER: 1998:323225 BIOSIS

Searcher : Shears 571-272-2528

10/712423

DOCUMENT NUMBER: PREV199800323225  
TITLE: Free radical-scavenging properties of olive oil polyphenols.  
AUTHOR(S): Visioli, Francesco [Reprint author]; Bellomo, Giorgio; Galli, Claudio  
CORPORATE SOURCE: Inst. Pharmacological Sci., Univ. Milan, Milan, Italy  
SOURCE: Biochemical and Biophysical Research Communications, (June 9, 1998) Vol. 247, No. 1, pp. 60-64. print.  
CODEN: BBRCA9. ISSN: 0006-291X.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 22 Jul 1998  
Last Updated on STN: 22 Jul 1998

AB Plants in the Mediterranean basin, such as vine and olive trees, have developed an array of antioxidant defenses to protect themselves from environmental stress. Accordingly, the incidence of coronary heart disease and certain **cancers** is lower in the Mediterranean area, where olive oil is the dietary fat of choice. As opposed to other vegetable oils, extra virgin olive oil, which is obtained by physical pressure from a whole fruit, is rich in phenolic components that are responsible for the particular stability of the oil. We have investigated the scavenging actions of some olive oil phenolics, namely hydroxytyrosol and oleuropein, with respect to superoxide anion generation, neutrophils respiratory burst, and hypochlorous acid. The low EC50s indicate that both compounds are potent scavengers of superoxide radicals and inhibitors of neutrophils respiratory burst: whenever demonstrated in vivo, these properties may partially explain the observed lower incidence of CHD and **cancer** associated with the Mediterranean diet.

FILE 'MARPAT' ENTERED AT 12:38:16 ON 03 MAR 2006  
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FILE CONTENT: 1969-PRESENT (VOL 144 ISS 9 (20060224/ED))

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1969-1987

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

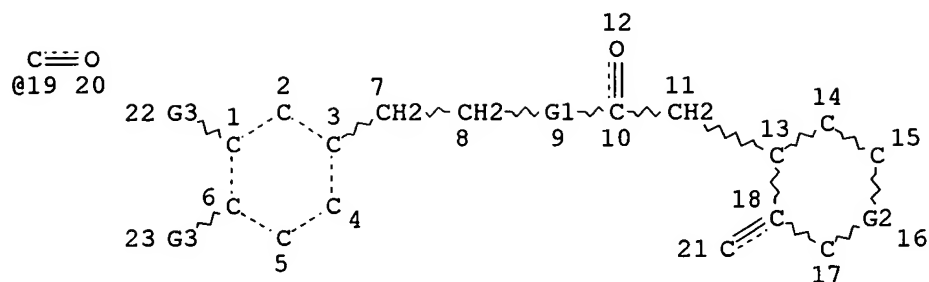
US 2006014764 19 JAN 2006  
DE 2020050148977 22 DEC 2005  
EP 1605533 14 DEC 2005  
JP 2005353222 22 DEC 2005  
WO 2006003494 12 JAN 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

L3 STR

10/712423



VAR G1=O/S/CH2/19  
 VAR G2=O/S/CH2/19  
 VAR G3=OH/N/S  
 NODE ATTRIBUTES:  
 CONNECT IS X2 RC AT 15  
 CONNECT IS M3 RC AT 17  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:  
 ECLEVEL IS LIM ON ALL NODES  
 ALL RING(S) ARE ISOLATED

L17 7 SEA FILE=MARPAT SSS FUL L3 (MODIFIED ATTRIBUTES)  
 L18 4 SEA FILE=MARPAT ABB=ON PLU=ON L17/COMPLETE

*Retrieves only  
 citations w/ complete  
 iterations*

L18 ANSWER 1 OF 4 MARPAT COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 140:400046 MARPAT  
 TITLE: Methods for inhibiting cancer and scar formation  
 INVENTOR(S): Hamdi, Hamdi K.; Castellon, Raquel  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of  
 U.S. 657,414.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004097428	A1	20040520	US 2003-712423	20031113
US 2003004117	A1	20030102	US 2002-153003	20020522
US 6632798	B2	20031014		
US 2004048808	A1	20040311	US 2003-657414	20030908
CA 2508786	AA	20040624	CA 2003-2508786	20031204
WO 2004053067	A2	20040624	WO 2003-US38564	20031204
WO 2004053067	A3	20040819		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,

Searcher : Shears 571-272-2528



10/712423

GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,  
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,  
MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,  
SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU,  
ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,  
DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
MR, NE, SN, TD, TG

EP 1569516 A2 20050907 EP 2003-812800 20031204

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,  
PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:

US 2002-153003 20020522  
US 2002-431780P 20021209  
US 2003-657414 20030908  
US 2001-292947P 20010523  
US 2003-712423 20031113  
WO 2003-US38564 20031204

AB Methods are disclosed for inhibiting cancer, scar formation,  
disrupting the cellular cytoskeleton, and conferring resistance from  
infection are disclosed. Such methods comprise the administration of  
oleuropein and/or the products of its hydrolysis in therapeutically  
effective amts. To that end, a variety of pharmaceutical formulations  
and routes of administration are disclosed and may be utilized to  
treat a wide variety of diseases.

L18 ANSWER 2 OF 4 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 140:229477 MARPAT

TITLE: Methods using oleuropein and related compounds for  
inhibiting angiogenesis, and therapeutic use

INVENTOR(S): Hamdi, Hamdi K.; Tavis, Jeffrey H.; Castellon,  
Raquel

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of  
U.S. Ser. No. 153,003.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004048808	A1	20040311	US 2003-657414	20030908
US 2003004117	A1	20030102	US 2002-153003	20020522
US 6632798	B2	20031014		
US 2004097428	A1	20040520	US 2003-712423	20031113
			US 2001-292947P	20010523
			US 2002-153003	20020522
			US 2002-431780P	20021209
			US 2003-657414	20030908

PRIORITY APPLN. INFO.:

AB Methods for inhibiting angiogenesis are disclosed which comprise  
administering oleuropein and/or the products of its hydrolysis in  
therapeutically effective amts. The methods and compns. of the  
invention are particularly effective in inhibiting the vascularization  
of endothelial cells, and may be utilized to treat a wide variety of  
cancers, ocular diseases, and inflammatory conditions.

10/712423

L18 ANSWER 3 OF 4 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 137:380057 MARPAT  
 TITLE: Methods for inhibiting angiogenesis using  
 oleuropein and its hydrolysis products  
 INVENTOR(S): Hamdi, Hamdi K.; Tavis, Jeffrey H.; Castellon,  
 Raquel  
 PATENT ASSIGNEE(S): USA  
 SOURCE: PCT Int. Appl., 54 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094193	A1	20021128	WO 2002-US16191	20020522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2447231	AA	20021128	CA 2002-2447231	20020522
EP 1397105	A1	20040317	EP 2002-739332	20020522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009922	A	20040727	BR 2002-9922	20020522
CN 1531435	A	20040922	CN 2002-812125	20020522
JP 2005508856	T2	20050407	JP 2002-590914	20020522
ZA 2003008763	A	20040526	ZA 2003-8763	20031111
PRIORITY APPLN. INFO.:			US 2001-292947P	20010523
			WO 2002-US16191	20020522
AB Methods for inhibiting angiogenesis comprise administering oleuropein and/or the products of its hydrolysis in therapeutically effective amts. The methods and comps. of the present invention are particularly effective in inhibiting the vascularization of endothelial cells, and may be utilized to treat a wide variety of cancers, ocular diseases, and inflammatory conditions. For example, anti-angiogenic properties of oleuropein in the adult mouse ear model were illustrated. Oleuropein potently inhibited existing blood vessels from sprouting. The burn area is in fact devoid of blood vessels.				
REFERENCE COUNT:	5	THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L18 ANSWER 4 OF 4 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 125:96055 MARPAT  
 TITLE: Antiviral compositions comprising secoiridoids  
 obtained from Oleaceae  
 INVENTOR(S): Fredrickson, William R.  
 PATENT ASSIGNEE(S): Strecker, Robert B., USA  
 SOURCE: PCT Int. Appl., 20 pp.

Searcher : Shears 571-272-2528

10/712423

CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

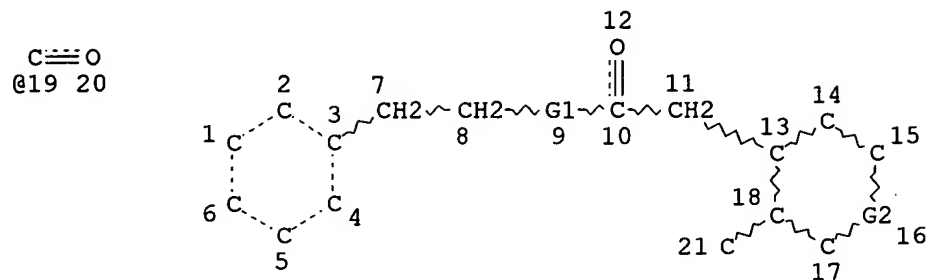
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9614064	A1	19960517	WO 1995-US14056	19951103
W:	AL, AM, AT, AU, BB, BG, BR, BY, CA, CH; CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9641391	A1	19960531	AU 1996-41391	19951103
US 6117844	A	20000912	US 1996-668324	19960626
US 6455580	B1	20020924	US 2000-659204	20000911
PRIORITY APPLN. INFO.:			US 1994-335138	19941107
			WO 1995-US14056	19951103
			US 1996-668324	19960626

AB A method of treatment of diseases of viral origin comprises oral or parenteral administration of an antiviral amount of a naturally occurring secoiridoid or derivs. thereof from plants of the family Oleaceae. Preferred oral dosage forms include the secoiridoid oleuropein in pure form or as a component of dried plant material of Olea europaea or a dried extract thereof and a pharmaceutically acceptable carrier. Dried leaves of Olea europaea was suspended in 2 volume of red wine and held at room temperature for 7-10 days with periodic stirring. Filtration of the mixture provided a tincture containing 88 mg of oleuropein/oz of fluid. The antiviral efficacy of above composition in treatment of six subjects afflicted with herpes virus infection is reported.

FILE 'HOME' ENTERED AT 12:40:51 ON 03 MAR 2006

10/712423

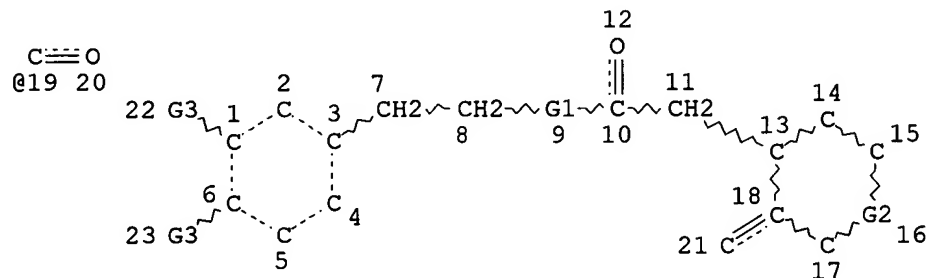
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DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE  
L2 ( 132)SEA FILE=REGISTRY SSS FUL L1  
L3 STR



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CONNECT IS X2 RC AT 15  
CONNECT IS M3 RC AT 17  
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 23

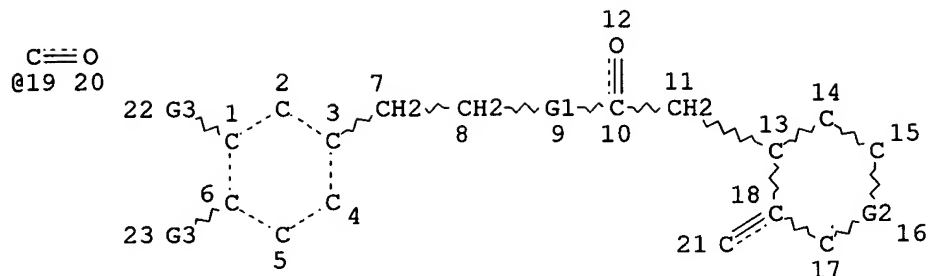
STEREO ATTRIBUTES: NONE  
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100.0% PROCESSED 127 ITERATIONS  
SEARCH TIME: 00.00.01

32 ANSWERS

10/712423

L3 STR



VAR G1=O/S/CH2/19  
VAR G2=O/S/CH2/19  
VAR G3=OH/N/S  
NODE ATTRIBUTES:  
CONNECT IS X2 RC AT 15  
CONNECT IS M3 RC AT 17  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:  
ECLEVEL IS LIM ON ALL NODES  
ALL RING(S) ARE ISOLATED

L17 7 SEA FILE=MARPAT SSS FUL L3 (MODIFIED ATTRIBUTES)  
L18 4 SEA FILE=MARPAT ABB=ON PLU=ON L17/COMPLETE

(FILE 'REGISTRY' ENTERED AT 12:27:31 ON 03 MAR 2006)  
DEL HIS Y  
ACT GEMB2/A

L1 STR  
L2 ( 132)SEA SSS FUL L1  
L3 STR  
L4 32 SEA SUB=L2 SSS FUL L3

FILE 'REGISTRY' ENTERED AT 12:30:53 ON 03 MAR 2006  
D QUE STAT

FILE 'CAPLUS' ENTERED AT 12:30:53 ON 03 MAR 2006  
L5 540 SEA ABB=ON PLU=ON L4  
L6 30 SEA ABB=ON PLU=ON L5 AND (?CANCER? OR ?CARCIN? OR  
?TUMOUR? OR ?TUMOR? OR ?NEOPLAS?)  
L7 13 SEA ABB=ON PLU=ON L6 NOT (PY=>2002 OR PD=>20021209)  
L\*\*\* DEL 4 S L6 AND HAMDI ?/AU

Searcher : Shears 571-272-2528

10/712423

D TI AU 1-4  
SEL HIT L8 RN

FILE 'REGISTRY' ENTERED AT 12:31:55 ON 03 MAR 2006  
L\*\*\* DEL 4 S E30-33

FILE 'CAPLUS' ENTERED AT 12:33:11 ON 03 MAR 2006  
DEL SEL Y  
SEL HIT L8 2 RN

FILE 'REGISTRY' ENTERED AT 12:33:26 ON 03 MAR 2006  
L\*\*\* DEL 2 S E1-2  
D SCAN

FILE 'CAPLUS' ENTERED AT 12:33:43 ON 03 MAR 2006  
SEL HIT L7 1-13 RN  
D L7 1-13 IBIB ABS HITSTR

FILE 'CAOLD' ENTERED AT 12:34:32 ON 03 MAR 2006  
L8 2 SEA ABB=ON PLU=ON L4  
D 1-2

FILE 'USPATFULL' ENTERED AT 12:34:48 ON 03 MAR 2006  
L9 74 SEA ABB=ON PLU=ON L4  
L10 27 SEA ABB=ON PLU=ON L9 AND (?CANCER? OR ?CARCIN? OR  
?TUMOUR? OR ?TUMOR? OR ?NEOPLAS?)  
L11 3 SEA ABB=ON PLU=ON L10 NOT (PY=>2002 OR PD=>20021209)  
D 1-3 IBIB ABS

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L\*\*\* DEL 406 S L4

FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 12:36:35 ON 03 MAR 2006  
L12 406 SEA ABB=ON PLU=ON L4  
L13 50 SEA ABB=ON PLU=ON L12 AND (CANCER? OR CARCIN? OR TUMOUR?  
OR TUMOR? OR NEOPLAS? OR ANTICANCER? OR ANTICARCIN? OR  
ANTITUMOUR? OR ANTITUMOR? OR ANTINEOPLAS?)  
L14 35 DUP REM L13 (15 DUPLICATES REMOVED)  
D KWIC  
L15 0 SEA ABB=ON PLU=ON L12(L) (CANCER? OR CARCIN? OR TUMOUR?  
OR TUMOR? OR NEOPLAS? OR ANTICANCER? OR ANTICARCIN? OR  
ANTITUMOUR? OR ANTITUMOR? OR ANTINEOPLAS?)  
D L14 1-35 IBIB ABS

FILE 'MARPAT' ENTERED AT 12:38:16 ON 03 MAR 2006  
D QUE L3  
L16 0 SEA SSS SAM L3 (MODIFIED ATTRIBUTES)  
L17 7 SEA SSS FUL L3 (MODIFIED ATTRIBUTES)  
L18 4 SEA ABB=ON PLU=ON L17/COMPLETE  
D QUE STAT  
D 1-4 .BEVMAR1

FILE 'HOME' ENTERED AT 12:40:51 ON 03 MAR 2006  
D QUE STAT L4  
D QUE STAT L18

#### FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file

Searcher : Shears 571-272-2528

10/712423

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STRUCTURE FILE UPDATES: 2 MAR 2006 HIGHEST RN 875740-40-2  
DICTIONARY FILE UPDATES: 2 MAR 2006 HIGHEST RN 875740-40-2

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMI  
for details.

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predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

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FILE COVERS 1907 - 3 Mar 2006 VOL 144 ISS 11  
FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply  
They are available for your review at:

<http://www.cas.org/infopolicy.html>

#### FILE CAOLD

FILE COVERS 1907-1966  
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate  
substance identification. Title keywords, authors, patent  
assignees, and patent information, e.g., patent numbers, are  
now searchable from 1907-1966. TIFF images of CA abstracts

Searcher : Shears 571-272-2528

10/712423

printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Mar 2006 (20060302/PD)

FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)

HIGHEST GRANTED PATENT NUMBER: US7007305

HIGHEST APPLICATION PUBLICATION NUMBER: US2006048257

CA INDEXING IS CURRENT THROUGH 28 Feb 2006 (20060228/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Mar 2006 (20060302/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

FILE MEDLINE

FILE LAST UPDATED: 2 MAR 2006 (20060302/UP). FILE COVERS 1950 TO DAT

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).

See also:

<http://www.nlm.nih.gov/mesh/>

[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)

[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.ht](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht)

[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT

FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 1 March 2006 (20060301/ED)

FILE EMBASE

FILE COVERS 1974 TO 24 Feb 2006 (20060224/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MARPAT



10/712423

FILE CONTENT: 1969-PRESENT (VOL 144 ISS 9 (20060224/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1969-1987

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2006014764	19	JAN	2006
DE	2020050148977	22	DEC	2005
EP	1605533	14	DEC	2005
JP	2005353222	22	DEC	2005
WO	2006003494	12	JAN	2006

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Gembel (SIS) Examiner #: 80889 Date: 2/22/06  
Art Unit: 16/4 Phone Number: 2-8604 Serial Number: 10/712 423  
Location (Bldg/Room#): 3A44 (Mailbox #): 3C70 Results Format Preferred (circle): PAPER DISK  
\*\*\*\*\*

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Methods of inhibiting cancer

Inventors (please provide full names): Hamidi et al

Earliest Priority Date: 12/09/02

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

① Please search compound of claim 1 for  
the treatment of cancer.  
where R<sub>4</sub>

X<sub>3</sub>

R<sub>5</sub>

X<sub>1</sub>

R<sub>1</sub>

R<sub>2</sub>

② claim 9

STAFF USE ONLY

Type of Search

Vendors and cost where applicable

Searcher: Beverly 2528 NA Sequence (#)

STN Dialog

Searcher Phone #: \_\_\_\_\_ AA Sequence (#)

Questel/Orbit Lexis/Nexis

Searcher Location: \_\_\_\_\_ Structure (#)

Westlaw WWW/Internet

Date Searcher Picked Up: \_\_\_\_\_ Bibliographic

In-house sequence systems

Date Completed: \_\_\_\_\_ Litigation

Commercial Oligomer Score/Length  
Interference SPDI Encode/Transl  
Other (specify)

Prep & Review Time: \_\_\_\_\_ Fulltext

Online Time: \_\_\_\_\_ Other